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RISK FACTORES ASSOCIATED THE MORTALITY OF THE CERVICAL CANCER IN NORTHEASTERN BRAZIL: A RETROSPECTIVE STUDY

***[1]Francisca Bruna Arruga Aragão, [2]Joelmara Furtados dos Santos Pereira, [3]Quesia Rodrigues Furtado, [4]Gerusinete Rodrigues Bastos dos Santos, [5]Franco Celso da Silva Gomes, [6]Givaldo de Jesus Pinheiro Lopes, [7]José Eduardo Batista, [8]Marcelino Santos Neto, [9]Ana Hélia de Lima Sardinha, [10]Jaqueline Diniz Pinho, [11]Paula Tâmara Vieira Teixeira Pereira, [12]Andréa Dias Reis and [13]Rodrigo Lopes da Silva**

[1]Nursing school of Ribeirão Preto - EERP, University of São Paulo, Ribeirão Preto, SP, Brazil
[2]Postgraduate Program in Adult Health at the Federal University of Maranhão – UFMA, São Luís, MA, Brazil
[3]Universidad Privada Latino Americana - UPAL, Cochabamba, Bolívia
[4]Postgraduate Program in Adult Health at the Federal University of Maranhão – UFMA, São Luís, MA, Brazil
[5]Postgraduate Program in Adult Health at the Federal University of Maranhão – UFMA, São Luís, MA, Brazil
[6]Nurse, Specialist, Family Health at the Federal University of Maranhão – UFMA, São Luís- MA, Brazil
[7]Department of Pathology at the Federal University of Maranhão (UFMA), São Luís, MA, Brazil
[8]Department of Nursing at the Federal University of Maranhão (UFMA), Imperatriz, MA, Brazil
[9]Department of Nursing at the Federal University of Maranhão– UFMA, São Luís, MA, Brazil
[10]Postgraduate Program in Genetics and Molecular Biology (PPGBM), Federal University of Pará (UFPA), Belém, Brazil
[11]Master's Degree and Nutritionist of Laboratory of Immunophysiology, Federal University of Maranhão Postgraduate Program in Adult Health at the Federal University of Maranhão – UFMA, São Luís, MA, Brazil
[12]Post-graduation Program in Movement Sciences of São Paulo State University, São Paulo, Brazil
[13]Postgraduate Program in Adult Health at the Federal University of Maranhão – UFMA, São Luís, MA, Brazil

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****Corresponding author:***
Francisca Bruna Arruga Aragão

ABSTRACT

Background: Cervical cancer (CU) is the third most prevalent cancer in women worldwide and Pap smear is a simple, effective and inexpensive technology to modify the rates of prevention, prevalence, and mortality of CU and its precursor lesions. All lesions are curable in up to 100% of cases when treated early and adequately. **Objective:** Identify the profile of patients with Cervical Cancer, assisted at a Center for High Complexity in Oncology in Northeastern Brazil.**Methods:** It sought to find retrospective data from patients diagnosed with anatomopathological cervical cancer. Clinical data were obtained through the search of reports at Center for High Complexity in Oncology, where the following variables were considered: age, ethnicity, educational level, staging, family history of cancer, alcohol and cigarette consumption. **Results:** 3,235 cases were diagnosed. The patients' age was 47.5 years (± 12.8). There was a prevalence of yellow women, 1,312 (40.55%). Low schooling was observed in this sample. Staging II was present in 976 (30.17%) cases, followed by staging III in 962 (29.73%), 1,430 women (44.20%) were alcoholics, and 1,128 (34.87%) smoked. The percentage of mortality in the study years was 5.20%, 18.92%, 5.03%, 11.67%, 17.72%, 15.09% and 18.92%, respectively. **Conclusions:** the profile of uterine cancer is found in stages II and III. The sample consisted of women of low schooling, a known risk factor for the disease. In addition, the mortality rate has increased over the years, except in the year 2008.

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INTRODUCTION

Cervical cancer (CU) is the third most prevalent cancer in women worldwide, with about 528,000 cases per year (Ferlay, 2015).

CU is a significant public health problem mainly due to increased exposure to risk factors and changes in the population's lifestyle (Noronha, 1999). It is a slow developmental disease with the necessary cause of infection by

the Human Papillomavirus (HPV) (Damacena, 2006 and Leyden, 2005). A possible explanation for the high prevalence rates in developing countries is the lack or inefficiency of screening programs. In Brazil, the screening strategy recommended by the Ministry of Health is the Pap smear, which was carried out primarily in women aged 25-64 years old. Also, since the early 2000s, prophylactic vaccines against HPV of subtypes 6, 11, 16 and 18 were available (Cancer, 2012). Pap smear is a simple, effective and inexpensive technology to modify the rates of prevention, prevalence, and mortality of CU and its precursor lesions, possible to detect neoplastic cells by vaginal smear (Silva, 2016). The precursor lesions of the CU are in different evolutionary degrees, from the cyto-histopathological point of view, being classified as cervical intraepithelial neoplasia (CIN) of degrees I (low-grade lesions), II and III (high-grade lesions). All lesions are curable in up to 100% of cases when treated early and adequately. When screening is performed within quality standards, it has 80% coverage for invasive cancer and, if the initial lesions are treated, the reduction in the rate of invasive cervical cancer can reach 90% (Silva, 2016 and Brasil, 2002). However, although it is almost entirely preventable, the coverage of this test in the Brazilian female population is still low (Eluf-Neto, 2001). Also, this cytological examination in the country has its recommended indication focusing only on women in the age group between 25 and 64 years old. Thus, the youngest and also susceptible women to the disease are often not covered by this crucial diagnostic-preventive measure, since they are also exposed to high risks of HPV infection, especially because of earlier sexual initiation (Sanches, 2017). Thus, the aim of this study was to identify the profile of patients with Cervical Cancer, assisted at a Center for High Complexity in Oncology in Northeastern Brazil.

METHODS

Study and Sample: This is a retrospective study, whose data were obtained from the survey of medical records of patients living in the state of Maranhão diagnosed with anatomopathological cervical cancer treated at a Center for High Complexity in Oncologybetween 2006 and 2012. The following variables were collected: age, ethnicity, educational level, staging, family history of cancer, alcohol and cigarette consumption. The inclusion criteria used in the study were based on patients of any age and gender, assisted at aCenter for High Complexity in Oncology with a diagnosis of CU between 2006 and 2012. Patient records without the information researched were not included in the study. Risk factor variables for 2010 could not be evaluated due to lack of data.All procedures and protocols undertaken were approved by the Ethics Committee (Protocol number. 1.502.349).

Data Analysis

Data were tabulated in a spreadsheet using the Microsoft Office Excel 2007 program, and absolute and relative frequencies (%), averages, medians and standard deviations were calculated for all variables addressed in this work. The chi-square test of association was used to measure the association between the mortality of the years and the other variables of the study (sociodemographic and clinical). Odds ratios and the confidence interval (95%) were calculated by the logistic regression model for all variables. The result was considered significant if the probability of error was ≤5% ($P < 0.05$).

RESULTS

In the study, there were 3,235 new cases of cervical cancer diagnosed from 2006 to 2012 in São Luís, MA, in women aged between 24 and 65 years old.

Table 1. Description of the epidemiological characteristics of the sample

Variables	2006 (n = 404)	2007 (n = 465)	2008 (n = 457)	2009 (n = 454)	2010 (n = 440)	2011 (n = 550)	2012 (n = 465)
Age	47.5±18.9	48.6±19.0	46.1±20.1	49.2±18.9	45.1±18.1	47.3±19.1	48.6±19.1
Ethnicity							
Caucasian	32 (8%)	69 (15%)	17 (4%)	50 (11%)	89 (20%)	73 (13%)	69 (15%)
Black	22 (5%)	29 (6%)	2 (0%)	14 (3%)	21 (5%)	31 (6%)	29 (6%)
Brown	167 (41%)	141 (30%)	0 (0%)	6 (1%)	21 (5%)	80 (15%)	141(30%)
Yellow	1 (1%)	183 (39%)	104 (23%)	261 (57%)	275 (63%)	305(56%)	183 (39%)
Ignored	182 (44%)	43 (9%)	334 (73%)	123 (27%)	34 (8%)	61(11%)	43 (9%)
Educationlevel							
None	9 (2%)	48 (10%)	46 (10%)	58 (13%)	95 (22%)	79 (14%)	48 (10%)
Elementary	8 (2%)	168 (36%)	114 (25%)	239 (53%)	208 (47%)	261 (47%)	168 (36%)
High school	2 (2%)	82 (18%)	22 (5%)	58 (13%)	67 (15%)	79 (14%)	82 (18%)
Highereducation	1 (0%)	75 (16%)	3 (1%)	54 (12%)	50 (11%)	63 (11%)	75 (16%)
Ignored	384 (94%)	92 (20%)	272 (59%)	45 (10%)	20 (5%)	68 (12%)	92 (20%)
Staging							
I	56 (14%)	59 (13%)	59 (13%)	98 (22%)	70 (16%)	60 (11%)	59 (13%)
II	127 (32%)	121 (26%)	152 (33%)	132 (29%)	141 (32%)	187 (34%)	121 (26%)
III	90 (22%)	163 (35%)	98 (21%)	123 (27%)	166 (38%)	164 (30%)	163 (35%)
IV	26 (6%)	46 (10%)	20 (4%)	23 (5%)	31 (7%)	41 (27%)	46 (10%)
Ignored	105 (26%)	76 (16%)	128 (28%)	78 (20%)	32 (7%)	98 (18%)	76 (16%)
Family historyof câncer							
Yes	17 (4%)	96 (21%)	86 (19%)	109 (24%)	89 (20%)	135 (25%)	96 (21%)
No	58 (14%)	104 (22%)	153 (33%)	192 (42%)	139 (32%)	169 (31%)	104 (22%)
Ignored	329 (81%)	265 (57%)	218 (48%)	153 (34%)	212 (48%)	246 (45%)	265 (57%)
Alcoholconsumption							
Yes	92 (23%)	234 (50%)	191 (42%)	177 (39%)	199 (45%)	303 (55%)	234 (50%)
No	18 (4%)	26 (6%)	42 (9%)	79 (17%)	22 (5%)	25 (5%)	26 (6%)
Ignored	294 (73%)	205 (44%)	224 (49%)	198 (44%)	219 (50%)	222 (40%)	205 (44%)
Cigaretteconsumption							
Yes	55 (14%)	189 (41%)	166 (36%)	124 (27%)	153 (35%)	252 (46%)	189 (41%)
No	65(16%)	75 (16%)	71 (16%)	150 (33%)	102 (23%)	87 (16%)	75 (16%)
Ignored	284 (70%)	201 (43%)	220 (48%)	180 (40%)	185 (42%)	211 (38%)	201 (43%)

The Biological social and clinical data of the study are shown in (Table 1), with the absolute frequency and the percentages of the clinical variables. The mean age of the patients at the time of diagnosis was 47.5 years old (± 12.8).

Regarding the prevalence of CU between 2006 and 2012, it was verified that 2011 was the year with the highest incidence, with 550 positive diagnoses. As for ethnicity, it was observed that 1,312 (40.55%) women declared to be yellow, while 556 (17.18%) declared to be brown, 399 (12.33%) declared to be Caucasian, and 148 (4.57%) declared to be black. Of the patients analyzed, 820 (25.34%) did not declare their ethnicity. Low education level was observed in this sample. There were 335 women (10.35%) who declared to be illiterate, 1,166 (36.04%) patients studied until elementary school, 392 (12.11%) had a high school education level, 323 (9.98%) had a higher education level, and 728 (22.50%) women did not answer this question in the questionnaire. Regarding alcohol consumption, it was found that approximately 1,430 women (44.20%) reported consuming these beverages, while 238 (7.36%) reported not drinking and 1,567 (48.44%) women did not answer their consumption profile. Regarding the tobacco use, there were 1,128 (34.87%) women in this study who reported smoking, 625 (19.32%) reported they did not smoke and 1,482 (45.81%) did not answer this question. According to the family history of cancer, 620 (19.16%) of the patients reported that there are cases of CU among their relatives, 919 (28.41%) answered that there were no cases of CU in the family and 1,696 (52.42%) did not answer this question. Staging II was present in 976 (30.17%) of the cases, followed by staging III with 962 (29.73%), stage I with 461 (14.25%) and staging IV with 316 patients (9.76%). The stages I and II were considered "early stages", and staging III and IV were considered as "late stage". Of the patients analyzed, 593 (18.33%) did not report the staging of CU in the analysis. The statistical analysis of the association between sociodemographic and clinical variables with the percentage of mortality was shown in (Table 2). It was observed that for all the evaluated years, risk factors such as alcohol consumption, cigarette consumptionand family history were not associated with the mortality rate, with no significant difference (P > 0.05) between the variables.

Table 2. Risk factors described as associated with mortality in women with cervical cancer treated at a Center for High Complexity in Oncology (CACON) from 2006 to 2012

Variables	Adjusted OR	CI 95%	p value
Cigaretteconsumption			
2006	0.40	0.08-2.22	0.29
2007	1.07	0.63-1.78	0.82
2008	2.21	0.48-9.51	0.30
2009	1.14	0.58-2.14	0.72
2011	0.89	0.53-1.55	0.73
2012	1.03	0.60-1.76	0.91
Alcoholconsumption			
2006	0.26	0.04-1.74	0.14
2007	0.97	0.34-2.72	0.95
2008	0.41	0.11-1.45	0.15
2009	0.84	0.37-1.87	0.67
2011	1.56	0.44-5.44	0.47
2012	0.97	0.34-2.72	0.95
Family history			
2006	1.07	0.10-11.06	0.94
2007	0.62	0.06-6.17	0.68
2008	1.01	0.28-3.58	0.97
2009	1.78	0.87-3.63	0.10
2011	1.01	0.51-2.01	0.96
2012	0.70	0.34-1.43	0.33

OR = odds ratio; CI = confidence interval;
The odds ratios and the confidence interal (95%) were calculated. The result was considered significant if the probability of error was ≤5% (P <0.05).

The percentage of mortality of patients living in the state of Maranhão with CU during 2006 to 2012 was 5.20%, 18.92%, 5.03%, 11.67%, 17.72%, 15.09% and 18.92%, respectively. The mortality rate of these women has increased over the years, except in the year 2008, as shown in Figure 1.

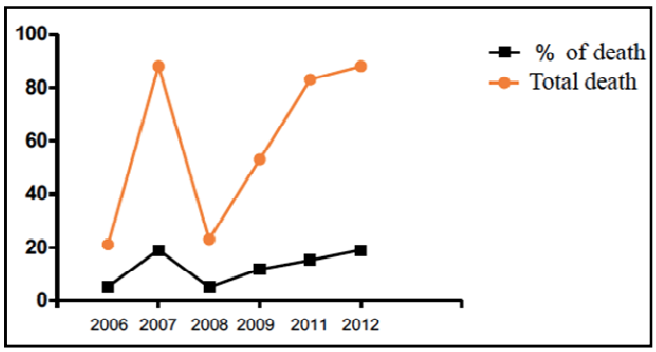

Figure 1. Mortality of patients living in the state of Maranhão with cervical cancer treated at Aldenora Bello Hospital between 2006 and 2012.São Luís, Maranhão, Brazil.

Age is a major risk factor in cancer. In this study, the mean age of the patients diagnosed with CU was 47.5 years old (± 12.8), which corroborates the current recommendations for the preventive exam that recommends its accomplishment in women between 25 and 64 years old (Maciel, 2011). Also, the prevalence of illiterate women with incomplete high school level represented 46.39% of the sample studied. According to a systematic review of the determinants and coverage of the Pap smear, failure to perform the examination, and consequently the non-treatment of precursor lesions were associated with low or high age, low level of education, low socioeconomic level and brown skin color (Martins, 2005), confirming the findings of this study. Women with a low educational level are at higher risk of developing cervical cancer (Da Silva, 2007), and the lower the education level, the greater the risk of advanced diagnosis of these tumors (Peres, 2007). In this study, 34.87% of patients with CU confirmed the use of tobacco. Other epidemiological studies report that smoking is one of the most important risk factors for CU development. Although the organs most directly exposed to tobacco smoke are the most affected, distant tissues, such as the bladder, cervix, and pancreas are also at risk (Albring, 2006). Therefore, smoking affects women's health in a broad way, and its effects affect not only the duration of life but also its quality. It is noteworthy that, since 1992, the World Health Organization (WHO) considers the persistence of HPV infection as the main risk factor for the development of the disease. However, there are cofactors for the development of cervical cancer, such as alcohol and family history (Aguiar, 2012).

In this study, the prevalence of patients with CUs was 44.20%, and 19.41% for patients reported that there were cases of CU in their relatives. It is worth highlighting that, since 1992, the World Health Organization (WHO) has considered the persistence of the Human Papillomavirus (HPV) infection as the main risk factor for the development of the disease, whose prevalence corresponds to around 90% of cases in Brazil and 73.3% in the state of Maranhão; (Da Silva, 2018), but there are cofactors for the development of cervical cancer, such as, for example, alcoholism and family history (Peres, 2007). In this study, the prevalence of alcoholic patients with CC was 44.20%, while 19.41% of patients reported that there were cases of CC among their relatives. Therefore, the high incidence of cervical cancer in the state of Maranhão may be

due to the high prevalence of viral infection. This leads us to reflect on the importance of vaccination as the main prophylactic measure. The variable clinical staging was related to the years of study. It was observed that staging II had a higher prevalence with 981 cases. The study with 96 cancer treatment institutions in the country showed that although the number of women arriving at institutions with cervical cancer in advanced staging is still large, this figure has been decreasing in recent years, but it is still far from reaching the parameters of developed countries (Thuler, 2005). In England, for example, only 23.8% of 382 registered cases are detected in stages III and IV.[20] Another survey conducted in the United States found only 7% of advanced cases with distant metastases (Leyden, 2005). The mortality rate of patients living in the state of Maranhão with CU during the study years was demonstrated in (Figure 1), presenting the highest indexes with 18.92% mortality in 2007 and 2012. For WHO, a coverage of 80% of cytopathological screening would be enough to impact morbidity and mortality indicators, which can be observed after four years of implementation of early detection actions, as in the State of Paraná (Bleggi, 2003). However, in other regions of the country, mortality rates by CU have been relatively high, although there are already theoretical knowledge and government programs sufficient to provide high rates of cure, CU remains a public health problem in Brazil (Ceolin, 2019).

In a study (Barbosa, 2016), performed in Brazilian regions and states from 1996 to 2010, based on secondary data collected from the Mortality Information System (SIM, as per its Portuguese acronym), it was found that, in Brazil, 89,764 deaths were registered due to malignant neoplasm of cervical uterus during the period from 1996 to 2010. In order to analyze cervical cancer mortality trends,it was adopted a method using the Joinpoint regression analysis with the Annual Percentage Change (APC), based on the trend of each segment. For this purpose, the states of Maranhão (APC= 7.1%) and Roraima (APC=5.7%) showed the highest trends of increase in rates among all Brazilian states, while the states of Acre (APC= -6.5%) and Rio Grande do Sul (APC= -4.1%) obtained the highest rates of reduction. Therefore, the increased percentage of deaths observed in this study has corroborated with work, (Pinho, 2003) which pointed outthat Maranhão was one of the states that obtained the highest trends of increase in mortality rates. According to studies on the determinants of CU screening coverage in Brazil, women with low educational level, low socioeconomic level, low family income, among other variables, different from the other women who seek to perform the examination by indication of professionals, usually seek the test when they present some gynecological symptom, or obstetric need (Pinho, 2003). It is worth highlighting that this study had limitations regarding the variables of risk factors of the year 2010, which could not be evaluated, due to the lack of the information in the chosen medical record and/or because the patient was in the hospitalization period.

Conclusions

The cervical cancer profile found in theNortheasternBrazilis mostly in stages II and III. Also, most of the sample was composed of women of low educational level, a risk factor is already known for the disease when related to the low socioeconomic status.

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