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Changes in the Epidemiological Profile of Patients with Cervical Cancer in a Reference Hospital between 2010 and 2019

Albuquerque Junior Ricardo BC¹; Gadelha Brenda MA¹; Enes Livia SRP¹; Santana Maria Letícia M¹; Carneiro Vandre CG^{2,3}; Bezerra; Artur LR^{1,3*}

¹Faculdade de Ciências Médicas of Universidade De Pernambuco, Recife, PE, Brazil.

²Department of pelvic surgery, Hospital de Câncer De Pernambuco, Recife, PE, Brazil.

³Instituto de Medicina Integral Professor Fernando Figueira, Recife, Brazil.

Abstract

Introduction: Cervical cancer is one of the most frequent tumors in the female population, with an estimate that it is the fourth most prevalent type worldwide. The study of cervical cancer is of great importance, as it is a very prevalent cancer, with an efficient screening strategy and a high rate of cure and response to treatment, if detected in the early stages.

Objective: To carry out a comparative analysis between the epidemiological, clinical and treatment of patients with cervical cancer between the years 2010 and 2019.

Methods: Cross-sectional, retrospective and quantitative study with 318 patients with cervical cancer treated in 2010 and 2019. Sociodemographic, reproductive, lifestyle and clinical variables were evaluated.

Results: 212 (66.67%) patients from 2010 and 106 (33.33%) from 2019 were included. The mean age of patients was 53.1 years. Comparing data from patients from 2019 with those from 2010, there was a reduction in parity means (4.8 versus 6.9, $p < 0.001$) and a reduction in the mean number of smokers (62.8% versus 65.7%, $p = 0.675$). The main symptom reported by the patients was bleeding (67.6%), followed by pelvic pain (17.6%), in both years analyzed. There was a 17.4% decrease in disease detection in the late phase and a 14.1% increase in the early phase ($p < 0.001$). In the period analyzed, squamous cell carcinoma was the most common (87.4%), however there was a decrease in the proportion of this histological type, representing 91.8% in 2010 and 78.6% in 2019 ($p = 0.001$).

Conclusions: Comparatively between the analyzed years, there were changes in the epidemiological profile of patients treated at the Hospital de Câncer de Pernambuco (HCP), with a decrease in parity, a greater number of patients with early diagnoses and a decrease in the proportion of patients with squamous carcinoma.

Keywords: Uterine cervical neoplasms; Neoplasm staging; Neoplasms by histologic type; Epidemiology; Risk Factors.

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Correspondance: Artur Lício Rocha Bezerra, Doctor in Health Sciences, Oncology by the Fundacao Antonio Prudente - Hospital A.C. Camargo Adjunct Professor of Medicine at the Universidade De Pernambuco, PE, Brazil.

Tel: +55-81-99996-8378; Email: artur.licio@terra.com.br

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Introduction

Cervical cancer is one of the most frequent tumors in the female population, with an estimate that it is the fourth most prevalent type worldwide; among countries with low and medium human development index (HDI) it is the second cancer in incidence among women [1-3].

Considering the estimates of the National Cancer Institute (INCA) for the years 2020 to 2022, 16,590 new cases are expected to occur in Brazil each year, with an estimated risk of 15.43 cases per 100,000 women [3].

Uterine cervical cancer is associated with persistent infection by some types of Human Papillomavirus (HPV), especially the high-risk ones, such as 16 and 18, which alone are responsible for about 70% of cervical cancers around the world [4]. Smoking and immunosuppression are cofactors that corroborate persistent infection in high-grade dysplasia [5].

The main risk factors linked to cervical cancer are the early onset of sexual activity, multiparity, having multiple sexual partners, age (with a maximum incidence peak between 45 and 49 years), use of oral hormonal contraceptives and herpes type II infections, chlamydia and socioeconomic status of patients [5,6].

Cervical cancer originates from precursor lesions, defined based on the thickness of the affected epithelium, degree of atypia and cell maturation [5]. The progression of these lesions to a neoplasm is, in general, slow [5]. The main histological types are: Squamous Cell Carcinoma (SCC), accounting for about 80% of cases, and adenocarcinoma for approximately 20% of cases, the etiology of both types being related to HPV infection [5,7]. Social programs for screening this neoplasm are effective, with a significant decrease in the incidence and morbidity and mortality of the disease [7,8]. The training of professionals and health services is extremely necessary, aiming at guiding and educating the population in general, regarding the clarification of risk factors and the importance of screening [9]. The lack of adherence to the preventive exam can be explained by factors such as: shame, fear of the exam and/or the possible results, little knowledge about the importance of prevention, non-recognition as a member of the risk group, sexual inactivity, socioeconomic and cultural level, among other aspects [9].

A study carried out in Recife showed that, between 2000 and 2004, approximately 85% of deaths from cervical cancer occurred in hospitals; among these hospitals, 90.2% belonged to the Sistema Único De Saúde (SUS) care network, thus reinforcing the higher mortality among women with lower socioeconomic status [10]. A higher frequency of death was also demonstrated among black women, housewives and residents of neighborhoods with low living conditions [10].

This study aims to map the epidemiological profile and the changes that occurred between 2010 and 2019 of patients with cervical cancer at a hospital in the public health system, the Hospital do Câncer de Pernambuco (HCP), located in the city of Recife, in the state of Pernambuco, seeking to elucidate risk factors, worsening and improving conditions, and treatment options. This investigation can help in the approach, understanding and construction of health indicators of a population, which can help in the analysis of patterns of evolution of cervical cancer [11].

Materials and methods

A cross-sectional, retrospective study with a quantitative approach was carried out at the HCP, a reference in the field of health care in the State and a highly complex center in oncology.

The research population consisted of patients with cervical cancer, aged 18 years or older, with TNM and /or FIGO staging and admitted to the Pelvis sector of the HCP in the period from January 1, 2010 to December 31, 2010 and from January 1, 2019 to December 31, 2019, reported in the Registro Hospitalar de Câncer (RHC) [5]. Exclusion criteria were having started treatment outside the HCP and having another associated neoplasm.

Based on case identification by RHC, 846 patients were screened. A total of 324 (38.3%) patients with pre-invasive lesions were excluded and also 150 (17.7%) patients because they had been referred to the hospital only for radiotherapy, 28 (3.3%) because of misclassification, 17 (2.0%) because they had another associated neoplasm and 9 (1.1%) because they did not perform staging. Thus, a total of 318 patients remained in the study, the total number of cases analyzed in this investigation.

Data collection, from the physical records, took place from June 2021 to March 2022. The information analyzed in the study were the sociodemographic variables: Age at diagnosis of cancer and origin; reproductive: Age at sexarch, number of pregnancies and deliveries, history of previous sexually transmitted infections (STD); related to life habits: smoking; clinical: Main complaint, tumor staging (early: IA1 - IIA; late: IIB - IVA; metastatic: IVB), histological type of tumor, degree of differentiation, performance of lymphadenectomy, total number of dissected and metastatic lymph nodes, radiotherapy, type of radiotherapy, chemotherapy, recurrence and site of recurrence.

The data obtained from the analysis of medical records were collected in data collection forms, organized in an Excel® spreadsheet and, subsequently, statistically analyzed using the SPSS® program, version 26.0 for Windows®. In the statistical analysis, numerical data are expressed as mean and standard deviation and categorical data as frequency (absolute and relative). Categorical variables were analyzed using the chi-square test.

The Mann-Whitney or Student's T tests were considered for categorical independent variables and for covariates. As for the quantitative independent variables, Pearson's or Spearman's Correlation Tests were considered. Statistical tests consider the value of P less than 0.05 as significant.

The research was approved by the Research Ethics Committee of the HCP under the opinion of nº 46754321.7.0000.5205, as required by Resolution nº 466/12 of the Conselho Nacional de Pesquisa, which regulates scientific research on human beings in Brazil.

Results

The mean age of patients at diagnosis was 53.7 years (± 13.8 years) in 2010, and from 53.1 years (± 15.6 years) in 2019 ($p=0.314$) (Table 1).

There was a statistically significant reduction in parity means between 2010 and 2019 (6.9 *versus* 4.8 children, $p < 0.001$) and

also in the number of pregnancies (6.1 versus 4.3, $p < 0.001$). There was no significant difference when assessing the age of the first sexarch, with the discrepancy between the mean ages of the two years studied being only 6 months - 17.5 years in 2010 (± 4 years) and 17 years in 2019 (± 3.8 years) ($p = 0.341$) (Table 1).

Regarding the analysis of sociodemographic issues, a greater balance of distribution was observed among patients residing in the Metropolitan Region of Recife (RMR) and in other places in 2019, when compared to 2010, although without statistical significance. Of the 142 patients analyzed, when searching for the year 2019, such distribution was 51 patients (48.6 %) residing in the RMR and 54 (51.4%) in other locations. In contrast, in 2010, the distribution was 91 patients (42.9%) versus 121 (57.1%), respectively ($p = 0.341$) (Table 1).

From the analysis of 121 patients with the acknowledge of STD prior to diagnosis of cancer, 43 patients from 2010 and 79 patients from 2019, an important disproportion was highlighted. In 2010, the disparity was 38 (92.9%) without previous STD versus 3 (7.1%) with previous STD. There was a slight percentage approximation in 2019, but still with significant dissymmetry: 75 (94.9%) without previous STD versus 4 (5.1%) ($p = 0.641$) (Table 1).

Table 1 also shows that of the total of the two years analyzed, 124 (64.2%) patients did not smoke. In 2010, the difference between smokers and non-smokers was 65 (65.7%) and 34 (34.3%), respectively. In 2019, the values found were 59 positive for smoking (62.8%) against 35 negative (37.2%) ($p = 0.675$).

Regarding clinical aspects, bleeding was the most common complaint both in 2010 and in 2019, although with a higher frequency, but not statistically significant, in 2019 (72.6 versus 65.1%, $p = 0.175$). Pelvic pain was more common in 2019 (25.5% versus 13.7%, $p = 0.009$) (Table 2).

Regarding staging, patients from 2019 were comparatively admitted more frequently at an early stage than patients from 2010 (24.5% versus 10.4%, $p < 0.001$). Late staging cases were 88.2% in 2010 and 70.8% in 2019 ($p < 0.001$). There were only 8 patients with metastatic disease at staging, 8 in 2019 and 3 in 2010 (Table 2).

In 2019, a higher frequency of adenocarcinomas was observed when compared to SCC (91.8% versus 78.6%, $p = 0.001$), while no statistical difference was observed in relation to the degree of histological differentiation, with a frequency of poorly differentiated tumors from 20.9% in 2019 and 13.9% in 2010 ($p = 0.145$) (table 2).

The 2019 patients underwent more lymphadenectomy than the 2010 patients (68.6 versus 9.8%, $p = 0.001$), with a similar mean number of lymph nodes dissected in both groups (5.4 ± 7.9 in 2010 and 8.0 ± 7.0 in 2019, $p = 0.178$) (Table 2).

Regarding the use of adjuvant treatment, there was no statistical difference between patients treated in 2010 and those treated in 2019. Most of them underwent, when indicated, radiotherapy associated with chemotherapy (Table 2).

During the study period, analyzing only the year 2010 and only 2019, 31 patients relapsed, 12 (11.3%) in 2019 and 19 (9%) in 2010 ($p = 0.504$). Locoregional recurrence was the most common in both periods ($p = 0.857$) (Table 3).

In the analysis of survival among cancer patients, in the 1-year period there was an increasing trend comparing the year 2019 with 2010 (94.2% versus 89.5%, $p = 0.367$). In the 2-year analysis, 97.4% of the patients from the year 2019 were alive, while in the 2010 group, all were alive in that period ($p = 0.575$). Only 51 patients were followed up for at least 2 years (Table 3).

Table 1: Sociodemographic, reproductive and lifestyle characteristics of the studied population.

Variable	Total n (%)	2010 n (%)	2019 n (%)	p - value
	n (%)	n (%)	n (%)	
Total	318 (100)	212 (66.67)	106 (33.33)	
Age (mean \pm standard deviation)	53.1 \pm 14.4	53.7 \pm 13.8	52 \pm 15.6	0.314*
Parity (mean \pm standard deviation)	6.2 \pm 4	6.9 \pm 4.2	4.8 \pm 3.2	<0.001*
Pregnancy (mean \pm standard deviation)	5.5 \pm 3.7	6.1 \pm 3.9	4.3 \pm 2.9	<0.001*
Sexarch (mean \pm standard deviation)	17.3 \pm 3.9	17.5 \pm 4	17 \pm 3.8	0.341*
Origin (n = 317)				0.341**
RMR	142 (44.8)	91 (42.9)	51 (48.6)	
Others	175 (55.2)	121 (57.1)	54 (51.4)	
Previous STD (n = 121)				0.641**
Not	114 (94.2)	39 (92.9)	75 (94.9)	
Yes	7 (5.8)	3 (7.1)	4 (5.1)	
Smoking (n = 193)				0.675**
Not	124 (64.2)	65 (65.7)	59 (62.8)	
Yes	69 (35.8)	34 (34.3)	35 (37.2)	

* = T-test; ** = Chi Square test; RMR: Metropolitan Region of Recife; STD: Sexually Transmitted Disease.

Table 2: Clinical, histological and therapeutic characteristics of the studied population.

Variable	Total	2010	2019	p - value
	n (%)	n (%)	n (%)	
Total	318 (100)	212 (66.67)	106 (33.33)	
Chief Complaint (n = 318)				
Bleeding	215 (67.6)	138 (65.1)	77 (72.6)	0.175**
Discharge	37 (11.6)	25 (11.8)	12 (11.3)	0.902**
Pelvic pain	56 (17.6)	29 (13.7)	27 (25.5)	0.009**
Asymptomatic	13 (4.1)	8 (3.8)	5 (4.7)	0.689**
Dyspareunia	-	-	-	
Staging (n = 318)				<0.001**
Early	48 (15.1)	22 (10.4)	26 (24.5)	
Late	262 (82.4)	187 (88.2)	75 (70.8)	
Metastatic	8 (2.5)	3 (1.4)	5 (4.7)	
Histological Type (n = 310)				0.001**
Squamous Carcinoma	271 (87.4)	190 (91.8)	81 (78.6)	
Adenocarcinoma and others	39 (12.6)	17 (8.2)	22 (21.4)	
Tumor differentiation (n = 257)				0.145**
Well differentiated and moderately differentiated	215 (83.7)	143 (86.1)	72 (79.1)	
Poorly differentiated	42 (16.3)	23 (13.9)	19 (20.9)	
Lymphadenectomy (n = 86)				<0.001**
Not	57 (66.3)	46 (90.2)	11 (31.4)	
Yes	29 (33.7)	5 (9.8)	24 (68.6)	
Total dissected lymph nodes	7.2 ± 7.3	5.4 ± 7.9	8.0 ± 7.0	0.178*
Total metastatic lymph nodes	0.4 ± 1.2	0.1 ± 0.3	0.5 ± 1.4	0.087*
Radiotherapy (n = 295)				0.154**
Not	14 (4.7)	7 (3.6)	7 (7)	
Isolated	54 (18.3)	41 (21)	13 (13)	
Associated with chemotherapy	210 (71.2)	134 (68.7)	76 (76)	
post-operative	17 (5.8)	13 (6.7)	4 (4)	
Type of Radiotherapy (n = 278)				0.144**
Brachytherapy	21 (7.6)	18 (9.6)	3 (3.3)	
External radiotherapy	28 (10.1)	17 (9.1)	11 (12.1)	
Brachytherapy and external radiotherapy	229 (82.4)	152 (81.3)	77 (84.6)	
Chemotherapy (n = 271)				0.416**
Not	50 (18.5)	33 (18.9)	17 (17.7)	
Associated with radiotherapy	218 (80.4)	139 (79.4)	79 (82.3)	
postoperative	3 (1.1)	3 (1.7)	0 (0)	
Recurrence (n = 318)				0.504**
No/No Information	287 (90.3)	193 (91)	94 (88.7)	
Yes	31 (9.7)	19 (9)	12 (11.3)	
Site of Recurrence (n = 31)				0.857**
Vaginal	6 (19.4)	3 (15.8)	3 (25)	
Regional	11 (35.5)	6 (31.6)	5 (41.7)	
Lung	5 (16.1)	3 (15.8)	2 (16.7)	
Bones	5 (16.1)	4 (21.1)	1 (8.3)	
Liver	3 (9.7)	2 (10.5)	1 (8.3)	
Others	1 (3.2)	1 (5.3)	0 (0)	

* = T-test ** = Chi Square test

Table 3: Survival analyses of the studied population.

Survival	Total	2010	2019	p - value
1 year				0.367**
Alive (with or without illness)	100 (91.7)	51 (89.5)	49 (94.2)	
Death (from cancer or not)	9 (8.3)	6 (10.5)	3 (5.8)	
2 years				0.575**
Alive (with or without illness)	50 (98.0)	12 (100.0)	38 (97.4)	
Death (from cancer or not)	1 (2.0)	0 (0.0)	1 (2.6)	

* = T-test ** = Chi Square test

Discussion

The patients included in the study had a mean age of 53.1 years. This average ranged 1.7 years, being lower in 2019, but with no statistical association. A study carried out in a public and tertiary hospital located in the Distrito Federal with 97 patients with cervical cancer treated between 2016 and 2019, had a mean age of 49 years (± 15.0) [12]. In a study conducted in the United States, between 2014 and 2016, the mean age was 50 years [13].

Among sociodemographic data cited in the literature, multiparity is considered a risk factor for uterine cervical neoplasia, a fact probably due to the lack of guidance on contraceptive methods, difficulty in accessing these methods and consequent greater possibility of exposure to viral and bacterial infections [5]. Our study shows a lower incidence of multiparity and number of pregnancies in 2019 when compared to 2010, which seems to be a consequence of a greater general awareness of the population in relation to this subject [6]. Although not statistically significant, there were fewer women outside the RMR being treated at the HCP in 2019 (when compared to 2010), which may be due to an improvement in oncological care in public services in other locations, such as, for example, in the cities of Caruaru and Petrolina (agreste and sertão, respectively, in the state of Pernambuco). On the other hand, in another Brazilian study that analyzed 5613 patients in the state of Minas Gerais, a significantly higher risk of death from cervical cancer was found in regions in the interior of the state when compared to the central region [15]. It is known that other sexually transmitted diseases, such as type II herpes infection and chlamydia, in addition to that produced by HPV, may act as cofactors in the etiopathogenesis of cervical cancer [4,7]. The present study shows that, both in 2010 and in 2019, the vast majority of patients did not report the presence of previous STD (Table 1). We believe that this may be related to the misinformation of these patients about the real past clinical situation [6]. In Brazil, there have been government projects for decades to discourage the habit of smoking, with awareness campaigns, prohibitions in public places, etc [16]. Almost 65% of patients in both 2010 and 2019 did not smoke. This is a positive aspect because smoking is a cofactor that contributes to persistent infection in high-grade dysplasia [5]. The results obtained in this study showed that bleeding continues to be the most common symptom related to cervical cancer, with an increase of 7.5% in 2019, when compared to 2010. Pelvic pain, which may or may not be associated, continues in second place as the most frequent symptomatology, also with an increase of 11.8% in 2019. There were no significant changes in the percentage of women who had discharge or asymptomatic

ones, compared between 2010 and 2019. There is a certain unanimity in the studies showing intermittent vaginal bleeding, associated or not with the sexual act, as being the most common complaint. common in uterine cervical cancer [5,8,9,14]. With regard to staging, a reduction in detection in the late phase of 17.4% was observed in the year 2019 and an increase of 14.1% of early detection in the same year. Diagnosis in the early stages of the disease is associated with improved survival, localized treatments and a greater chance of cure [1,5,7]. The data found in the study points to an improvement in the detection of the disease at an early stage, a very important fact for the management of cases of this neoplasm. The need for cervical cancer prevention practices, whether through encouraging and carrying out regular preventive exams, or through the application of the HPV vaccine, is fundamental in coping with this neoplasm [4,7,14].

SCC was the most frequent histological type, both in 2010 and in 2019 in the present study. However, there was a significant increase in other histological types, adenocarcinoma being the main one, when comparing the year 2010 (8.2%) with the year 2019 (21.4%). It is important to note that the increase in the proportion of cases of adenocarcinoma, with a decrease in SCC, has been occurring in recent decades in several countries around the world, mainly in developed ones [17,18]. Studies suggest that this is happening, among other factors, because of the cytology test, which is more effective in detecting SCC precursor lesions [14,17,18].

Older studies carried out in Brazil indicated incidences between 8 and 10% of adenocarcinoma in Porto Alegre, during the years 2005 and 2006 [19]. This incidence was 12% between the years 1999 and 2004, according to INCA data [20]. The INCA itself, in a more recent study evaluating patients treated between 2012 and 2014, shows an incidence of 16.1% of adenocarcinomas and 83.9% CEC [14]. In this study, some differences between the two histological types were identified; patients with adenocarcinoma had higher education, later sexarch, nulliparity or a maximum of two children, less frequent smoking and predominance of cancer diagnosis with earlier staging [14]. It is also worth noting that, compared to SCC, adenocarcinoma has a worse prognosis, with greater metastasis. lymph node, and lower overall survival and disease-free survival [18]. This aspect may also explain the higher number of lymphadenectomies in 2019, when compared to 2010, performed in the present investigation (Table 2).

Patients continue to be treated with surgery (radical hysterectomy) in the earliest stages, with or without adjuvant treatment (mainly radiotherapy). The present investigation shows a similar number of indications for adjuvant treatment between the years 2010 and 2019. Once again, this aspect may mean earlier staging in the population treated with cervical cancer at the HCP. Cases considered surgically unresectable, in which there is infiltration of the parametrium, are treated with radiotherapy-chemotherapy, currently the gold standard for these stages [5]. Due to our work being restricted to the years 2010 and 2019, with a very small follow-up of some patients, survival analysis is not feasible. However, similar relapse rates were observed in both periods (9% in 2010 and 11.3% in 2019) and a trend towards increased survival in 2019 when compared to 2010, but not statistically significant (94.2% versus 89.5%).

The trend towards better survival may be confirmed in future studies and may be related, as previously discussed, to earlier stages of the disease.

It is important to emphasize that this study has limitations inherent to a retrospective study. Based on physical medical records searches, the records do not always contain complete and readable data. Among the limitations of this research, we can mention the lack of exploration of some important factors such as the use of oral contraceptives, number of sexual partners and age at menopause. The analysis of patient survival between the different groups could complement and measure the impact of the changes that are taking place. Furthermore, this is a hospital cohort and does not represent what happened in the Recife city population cohort.

Conclusion

In the last ten years there has been a change in the epidemiological profile of HCP patients with cervical cancer, with a decrease in multiparity and a trend towards a more equitable distribution between patients from Recife and the interior of the state. Clinically, these women continue to have genital bleeding as the most common sign, but they were proportionally diagnosed with earlier diagnoses and there was a decrease in the magnitude of the difference between the incidence of the two most frequent histological subtypes (SCC and adenocarcinoma). The greater number of lymphadenectomies may be associated with this higher incidence of adenocarcinomas.

Declarations

Conflict of interests: The authors have no conflict of interest to declare.

Contributions: All authors made substantial contributions to the conception and design, data collection or analysis, and interpretation of data, writing of the article or critical review of the intellectual content, and final approval of the version to be published.

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