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# PERFIL EPIDEMIOLÓGICO DE MULHERES COM CÂNCER DE COLO DE ÚTERO TRATADAS EM HOSPITAL TERCIÁRIO

# EPIDEMIOLOGY OF WOMEN WITH CERVICAL CANCER TREATED IN A TERTIARY HOSPITAL

# PERFIL EPIDEMIOLÓGICO DE MUJERES CON CÁNCER DE CUELLO UTERINO TRATADAS EN HOSPITAL TERCIARIO

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## RESUMO

**Objetivo:** caracterizar o perfil epidemiológico das mulheres com câncer de colo uterino atendidas em um hospital de referência em oncologia. **Método:** Analisaram-se 906 casos de câncer de colo de útero, atendidos no período de 2000 a 2013. Foram utilizados os testes Qui-quadrado e Kruskal-Wallis, para a comparação das variáveis; para a análise dos tempos, foi utilizado o teste de Mann – Whitney e, para sobrevida, foram construídas curvas de Kaplan-Meier e comparadas via teste Log- Rank. **Resultados:** Das 906 mulheres analisadas, 68,6% possuíam ensino fundamental; 39,6% foram diagnosticadas em estádio clínico 0. O cruzamento entre escolaridade e estadiamento apontou que, no estádio 0 34,8%, possuíam ensino fundamental ou médio. A sobrevida global em cinco anos foi 56,5% e os casos diagnosticados em estádios avançados foram responsáveis pelo maior número de óbitos. **Conclusão:** A escolaridade influenciou no diagnóstico precoce, e o diagnóstico, em estádio avançado, ocasionou maior número de mortes.

**Descritores**: Neoplasias do Colo do útero; Perfil de Saúde; Enfermagem Oncológica; Sobrevivência; Prognóstico.

## ABSTRACT

**Objective:** to characterize the epidemiological profile of women with cervical cancer treated at a referral hospital for oncology. **Method:** 906 cases of cervical cancer attended between 2000 and 2013 were used. Chi-square and Kruskal-Wallis tests were used to compare the variables; the Mann - Whitney test was used for the analysis of the times and Kaplan - Meier curves were constructed for survival and compared using the Log - Rank test. **Results:** Of the 906 women analyzed, 68.6% had primary education; and 39.6% were diagnosed in clinical stage 0. The cross-study between schooling and staging showed that, in stage 0 and in 39.6% of the cases, 34.8% had elementary or middle school education. Overall 5-year survival was 56.5% and cases diagnosed in advanced stages were responsible for the highest number of deaths. **Conclusion:** The schooling influenced the early diagnosis and the diagnosis at an advanced stage caused a greater number of deaths.

**Descriptors**: Uterine Cervical Neoplasms; Health Profile; Oncology; Survivorship; Prognosis.

## RESUMEN

**Objetivo:** caracterizar el perfil epidemiológico de las mujeres con cáncer de cuello uterino atendidas en un hospital de referencia en oncología. **Método:** Se analizaron 906 casos de cáncer de cuello uterino, atendidos en el período de 2000 a 2013. Se utilizaron las pruebas Qui-cuadrado y Kruskal-Wallis para la comparación de las variables; para el análisis de los tiempos se utilizó la prueba de Mann-Whitney y para la supervivencia fueron construidas curvas de Kaplan-Meier y comparadas vía test Log-Rank. **Resultados:** De las 906 mujeres analizadas, el 68,6% poseía educación básica; El 39,6% fue diagnosticado en estadio clínico 0. El cruce entre escolaridad y estadificación apuntó que, en el estadio 0, el 39,6% de los casos, el 34,8% poseía educación básica o media. La supervivencia global en 5 años fue 56,5% y los casos diagnosticados en estadios avanzados fueron responsables del mayor número de muertes. **Conclusión:** La escolaridad influenció en el diagnóstico precoz y el diagnóstico en estadio avanzado ocasionó mayor número de muertes.

**Descriptores**: Neoplasias del Cuello Uterino; Perfil de Salud; Enfermería Oncológica; Supervivencia; Pronóstico.

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## INTRODUCTION

Cervical cancer is considered a worldwide public health problem because it plays an important role in women's morbidity and mortality, and is a challenge in public policies in developing countries[1].

Statistics indicate 530,000 new cases and 270,000 deaths worldwide each year due to cervical cancer[2] and it is estimated that, by 2030, this cancer is responsible for the deaths of 474,000 women, 95% of which occur in middle and low income countries[1]. In Latin America, the incidence of cervical cancer is considered one of the highest in the world, accounting for up to 25% of all cancers in women[4].

In Brazil, cervical cancer is the third most frequent tumor in the female population and, by 2018-2019, 16,370 new cases are expected. According to the Mortality Information System (MIS), the number of cervical cancer deaths in 2013 was 5,430 women[5].

Cervical cancer, diagnosed at an early stage, has a good prognosis. However, middle and low-income countries have geographical variation in the incidence and mortality of this cancer. These differences can be attributed to socioeconomic levels, poor access to screening tests and prevention programs, poor health conditions, among others[6]. Approximately 85% of UCC cases occur in the least developed countries of Latin America and especially those in the poorest regions of Africa, which have high incidence rates, while the United States, Canada, Australia, Japan and other countries. Europeans have the lowest rates. Mortality from this cancer varies up to 18 times between different regions of the world, with rates of less than two per 100,000 women in West Asia and 27.6 in East Africa[3].

Identifying the common characteristics and survival of women treated with cervical cancer in our services will assist in the planning and control of this cancer in our population. This study aimed to characterize the epidemiological profile of women with cervical cancer treated at a referral hospital in oncology.

## METHODOLOGY

This is a cross-sectional study conducted in a single hospital using secondary source data. This hospital is a tertiary level institution, which is characterized as large, of high complexity, being a reference for the Northeast region of São Paulo State, composed of four million inhabitants. Users of the Unified Health System (UHS) represent 97% of care.

For data collection, the Hospital Cancer Registry (HCR) database was used, which provides information for the Population-Based Cancer Registry (PBCR), which is an important support tool for the formulation of the National Cancer Policy of Oncological Care, health planning, quality assessment of care activity and as a resource for the elaboration of clinical research and scientific work[7]. All HCR data are from medical records of women who have been diagnosed with cervical cancer.

Women diagnosed with cervical cancer from January 2000 to December 2013 were considered for this study. Cervical cancer cases were identified in the database through the ICD-10 (International Classification of Diseases), with C53 (C53 · 0 – C53 · 1, C53 · 8 – C53 · 9) referring to this neoplasm. A total of 909 women diagnosed with cervical cancer were identified during the study period, and three were excluded because they were under 18 years of age, and the final number of cases analyzed was 906 women.

This study was organized according to the TMN System for the classification of malignant tumors and the treatment was categorized into surgery, radiotherapy, and chemotherapy and hormone therapy. The cases were evaluated according to the average age and age groups, stage of diagnosis and treatments received.

Overall survival at five years was estimated based on the date of the first diagnosis (the date of the anatomopathological examination result was used). For the last date of the woman's follow-up, the following were considered: date of death recorded in the woman's database or hospital record, or of her last service visit.

Data analysis was performed using the Statistical Package for Social Sciences program (SPSS 23.0) and included descriptive analysis and survival analysis. For descriptive analysis, means and standard deviations were used for quantitative variables, and absolute and percentage frequencies for categorical variables. To compare categorical variables in two or more groups, the chi-square test was used.

For the comparison of the mean ages, the Kruskal-Wallis test was used, which compared the means between all stages. For the analysis of waiting times, diagnosis and treatment, the Mann - Whitney test was used. For survival analysis, Kaplan-Meier curves were constructed and compared using the Log-Rank test. The test was performed at 95% confidence interval (95% CI), and $P < 0.05$ was considered statistically significant.

This study was approved by the Ethics Committee (CAAE 39451714.0.0000.5393) under opinion number 1,266,933 in compliance with the guidelines and standards for research involving human subjects, regulated by Resolution CNS 466/2012.

**RESULTS AND DISCUSSION**

Of the 906 cases analyzed, the results indicate that the age range ranged from 18 to 95 years, and the predominant age was 31 to 60 years, corresponding to 534 (58.9%) women, and the average was 48.8 years ( SD = 16.4 years). The age group outside the MS recommendation was analyzed, which showed that 47 (5.2%) of the study population diagnosed with cervical cancer was 18 to 24 years old and 170 (18.8%) were diagnosed over the age of 65, totaling 217 (24%) women diagnosed outside the program period. Of the women analyzed, 374 (41.3%) had completed elementary school (Table 1).

Table 1 - Distribution of cervical cancer cases, according to age and education. Ribeirão Preto, SP, Brazil, 2015.

| Variables | N | % |
|---|---|---|
| **Age** | | |
| **≤ 24** | 47 | 5.2 |
| From 25 to 30 | 98 | 10.8 |
| From 31 to 40 | 177 | 19.5 |
| From 41 to 50 | 174 | 19.2 |
| From 51 to 60 | 183 | 20.2 |
| From 61 to 64 | 57 | 6.3 |
| **≥ 65** | 170 | 18.8 |
| Education | | |
| Illiterate | 98 | 10.8 |
| Complete Elementary School | 374 | 41.3 |
| Incomplete Elementary School | 245 | 27.0 |
| Highschool | 140 | 15.5 |
| Higher education | 28 | 3.1 |
| Ignored | 21 | 2.3 |

Source: HRC.

Mean age similar to that observed was found in a study that outlined the epidemiological profile of 77,317 women with cervical cancer in Brazil from 2000 to 2009. The average age was 49.2 years and 55.3% of them were found to be under 50 years of age at diagnosis[8]. Also similar to the data found in a study conducted in Vitória - Espírito Santo, which analyzed women with initial staging, from 2000 to 2005, identifying the predominance of the age group between 40 and 59 years (49.3%)[9].

It is noteworthy that cervical cancer is rare in women up to 30 years old, and its incidence progressively increases until its peak in the 45 to 50 year old range[8], which points to the increase of age, as an important risk factor for this neoplasia[10].

The most observed clinical stage was stage 0, diagnosed in 359 (39.6%) women, but even so, it is noteworthy that 225 (24.8%) of them were diagnosed in advanced stages (III and IV). The most incident cell type in the women studied was Squamous Cell Carcinoma No Other Specification (NOS) (Table 2).

Among the treatment modalities, the most observed was surgery with 635 (70.1%), and the same woman may have undergone more than one treatment during the follow-up at the service (Table 2).

Table 2 - Distribution of cervical cancer cases, according to clinical stage, cell type, ICD and treatment. Ribeirão Preto, SP, Brazil, 2015.

| Variables | N | % |
|---|---|---|
| **Grouped clinical stage** | | |
| 0 | 359 | 39.6 |
| I | 137 | 15.1 |
| II | 169 | 18.7 |
| III | 145 | 16.0 |
| IV | 80 | 8.8 |
| X | 5 | 0.6 |
| Y | 11 | 1.2 |
| **Cell type** | | |
| Adenocarcinoma | 28 | 3.1 |
| Adenocarcinoma, NOS * | 50 | 5.5 |
| In situ squamous cell carcinoma, NOS | 56 | 6.2 |
| Carcinoma | 93 | 10.3 |
| In situ carcinoma, NOS | 80 | 8.8 |
| Squamous Cell Carcinoma, NOS | 370 | 40.8 |
| Grade III squamous intraepithelial neoplasia | 218 | 24.1 |
| Others | 11 | 1.21 |
| **Treatments**[†] | | |
| None | 35 | 3.9 |
| Surgery | 635 | 70.1 |
| Radiotherapy | 347 | 38.3 |
| Chemotherapy | 325 | 35.9 |
| Hormone Therapy | 13 | 1.4 |
| **ICD of metastases** [§] | | |
| C67 (malignant bladder cancer) | 17 | 20.5 |
| C34 (malignant neoplasm of the bronchi and lungs) | 13 | 15.7 |
| C22 (malignant neoplasm of the liver and biliary tract) | 11 | 13.3 |
| C48 (malignant neoplasm of retroperitoneum and peritoneum soft tissue) | 6 | 7.2 |
| C41 (malignant neoplasm of bones and articular cartilage) | 5 | 6.0 |
| Others[‡] | 31 | 37.4 |

Source: HRC. * NOS: No other specification. † The same woman may have had more than one treatment. ‡ Other metastatic sites: ovary, vagina, vulva, renal pelvis, colon, rectum, kidney, brain, medulla, thyroid, lymph nodes. § The same woman may have had more than one metastasis site.

It was observed that 46 (5%) women had metastasis, and among them, 28 (60.9%) had at least one site. The main sites were: bladder 17 (20.5%); lungs 13 (15.7%); liver 11 (13.3%); retroperitoneum and peritoneum six (7.2%) and bones five (6%). According to the norms of the Oncocentro Foundation of São Paulo (OFSP), the sites of neighboring organs affected by cancer are not classified as tumor invasion, but as metastasis[7].

A study that used data from the Population-Based Cancer Registry (PBCR) of four Brazilian state capitals, from 1990 to 2004, showed a tendency for a decrease in invasive cancer and the growth of carcinoma in situ among groups of women studied. That may indicate positive results of screening actions for cervical cancer in the cities of Fortaleza, Porto Alegre and São Paulo[11]. In this study, carcinoma in situ (stage 0) and stage I were diagnosed in

54.7% of women, similar to that for this type of lesion reported by INCA, where it is stated that currently 44% of diagnosed cases are cancer in situ[5].

Clinical stage 0, the most frequent among the women analyzed, can demonstrate that the health network that assists the municipalities, to which the service under study is a reference, has implemented appropriate actions in relation to screening. However, they need to review their behavior and improve the approach of these women, because the diagnosis at an advanced stage, unfortunately, still persists and presents a high rate of cervical cancer mortality in women. Considering that of the 906 patients 280 died due to cancer, that is, 30.9% of the study population, 24.8% are related to advanced stages, which evidenced the high mortality associated with these stages. They represent data that suggest opportunistic screening, which is characterized by the examination when the woman seeks the health service and, in addition, the late diagnosis also suggests insufficient quality of the services offered[12], which could be minimized if there was an organized screening program for cervical cancer in the country.

The analysis of the cases, according to clinical stage and education, showed that, at stage 0, there were 359 (39.6%) of women diagnosed with cervical cancer, and 41% had completed elementary school (Table 3).

Table 3 - Distribution of cervical cancer cases, according to clinical staging and education. Ribeirão Preto, SP, Brazil, 2015.

| ED/Education | Illiterate | Incomplete elementary school | Complete elementary school | Highschool | Higher education | Ignored |
|---|---|---|---|---|---|---|
| 0 | 21 | 103 | 144 | 68 | 15 | 8 |
| I | 14 | 35 | 57 | 21 | 6 | 4 |
| II | 26 | 42 | 66 | 31 | 2 | 2 |
| III | 22 | 38 | 63 | 13 | 3 | 4 |
| IV | 10 | 25 | 35 | 7 | 2 | 1 |
| X | 3 | 0 | 2 | 0 | 0 | 0 |
| Y | 2 | 2 | 7 | 0 | 0 | 0 |

Source: HRC.

The relationship between advanced clinical stages and education was also observed in a study aimed at analyzing the determinants of advanced-stage diagnosis in women with cervical cancer in Brazil; the main associated factor was the histological type “squamous cell carcinoma”. It was also found that the socioeconomic disparities present in the country are associated with the advanced stage of the disease; Women 50 years of age and over, living without a partner, black / with little education[9].

People with lower income and education, because they are the most exposed to risk factors and with less access to health information and services, are considered to be the most vulnerable to chronic non-communicable diseases, including cancer[13]. This association is likely to be a Brazilian sociodemographic reality, especially in women seeking care in the public health service[14].

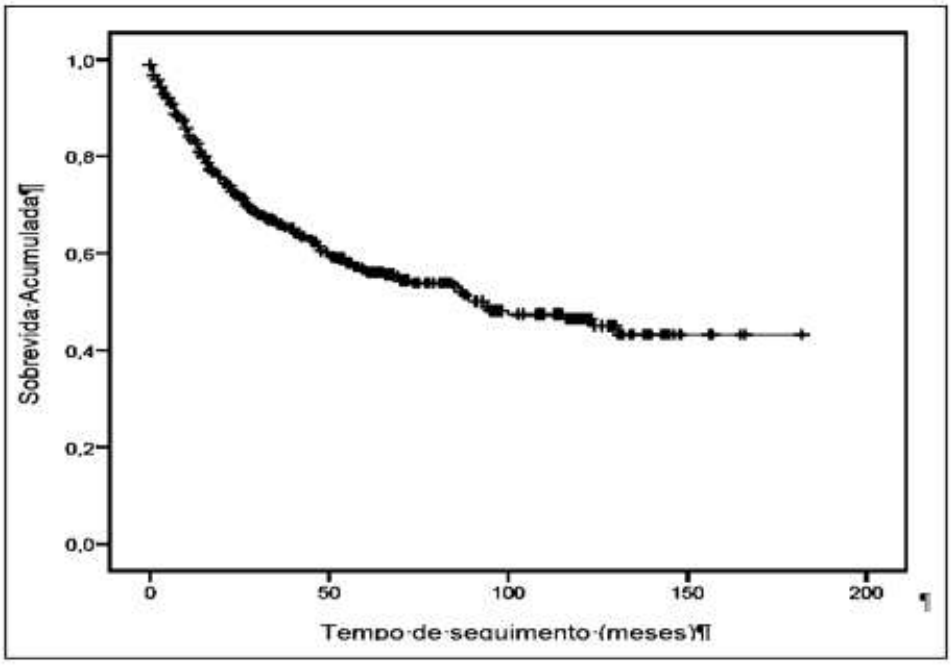
When the crossing between the clinical stage and death occurred, it was identified that the most advanced stages, III and IV, were responsible for the highest number of deaths among the studied women. Of the 359 (39.6%) women diagnosed at stage 0, only 14 (3.9%) died. Regarding the most advanced stages, of the 145 (16%) women in stage III, 87 (60%) died and 80 (8.8%) women diagnosed in stage IV, 67 (83.75%) died.

According to the statistical analyzes, it was observed that the average, in calendar days between the first consultation and the diagnosis of cervical cancer was 13.6 days (SD = 48.3); between diagnosis and initiation of treatment was 58.4 days (SD = 76.7) and from the first consultation to the last follow-up, whether due to medical discharge, death or treatment abandonment was 999.9 days, the minimum being zero and maximum 5538 days.

Of the 906 patients analyzed, 38 (4.2%) arrived at the service diagnosed with cancer and 868 (95.8%) without diagnosis. Therefore, for the analysis of these variables, the N of 868 women.

For survival analysis, the Log-Hank test was performed, which identified that at 60 months (five years), the probability of developing the event is 56.5% (Figure 1).

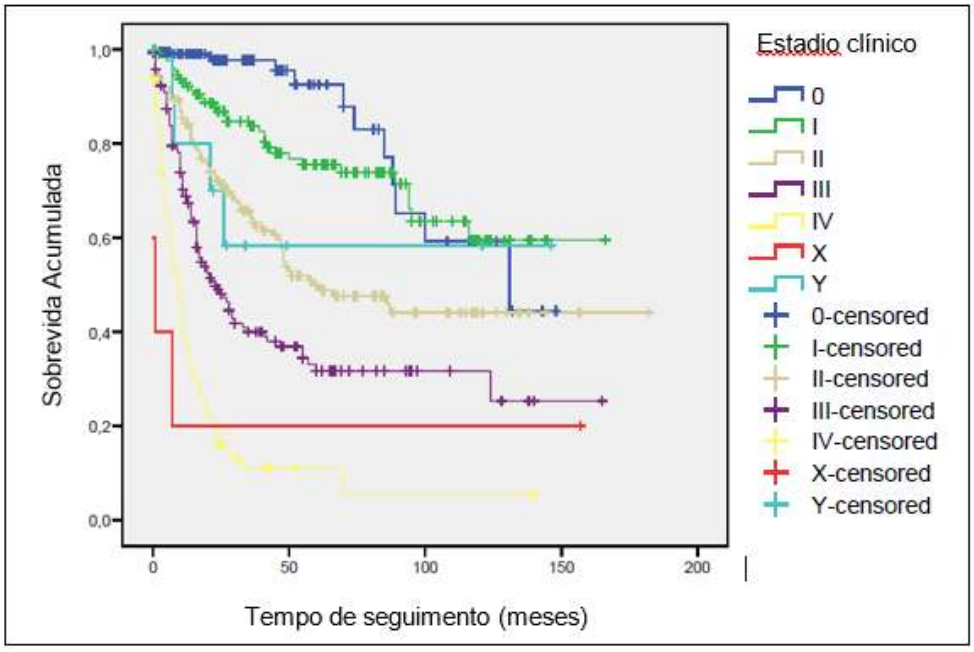
Figure 1 - Kaplan-Meier curve showing overall five-year survival of women with cervical cancer. Ribeirão Preto, SP, Brazil, 2015.




Cumulative survival - Time of follow up (months)

According to stage, survival was 96.1% for stage 0 and 16.3% for stage IV, showing that the more advanced the stage, the lower the survival (Figure 2).

Figure 2 - Kaplan-Meier curve showing overall five-year survival in relation to cervical cancer staging. Ribeirão Preto, SP, Brazil, 2015.




Cumulative survival - Time of follow up (months) - Clinical state

When performing the Mann-Whitney Test, for the observation time variable, one obtained p = 0.000, demonstrating that this variable was statistically significant. However, for the variables waiting time (p = 0.917) and diagnosis/ treatment time (p = 0.895), they were not statistically significant.

Globally, the five-year survival rate for cervical cancer has improved over the years, ranging from less than 50% to over 70%. In Brazil, from 2005 to 2009, survival was around 61%[5]. In this study, the overall five-year survival was 56.5%.

The average days between diagnosis and initiation of treatment for cervical cancer was 58.42 days, with SD = 76.72 days. This value is within the 60-day cancer treatment law (Law 12.732 / 12). This law came into force in 2012 and ensures that cancer patients begin treatment within 60 days after the inclusion of the disease in their medical records in UHS[15]. Since the value ranged from 53.31 days to 63.53 days, with a 95% confidence interval, the present law did not have a significant influence on the study population, since the values in days were already within the imposed period, by law even before it comes into force.

It is noteworthy that the implementation of prevention programs has been primarily responsible for modifying the incidence rate of cervical cancer in most countries undergoing a process of socioeconomic transition[16], where Brazil is. However, achieving the appropriate level of coverage of the target population remains a challenge for developing countries, and knowledge of the factors associated with carrying out Pap smears is essential to building strategies for reducing the incidence and mortality from cervical cancer[17]. In this sense, it is noted the need for a look focused on Primary Health Care, focused on tracking actions, expanding access and targeting the target population.

A study that analyzed information reported by Brazilian women between 25 and 64 years old, from the National Health Survey (NHS), conducted in 2013, in 26 Brazilian capitals and the Federal District and compared to information from the Vigitel System (System of Factors Surveillance System). Risk for Non-Communicable Diseases by Telephone Survey) concluded that Pap smear coverage is below 80% [18].

The success of screening actions depends on factors such as mobilization and information of the population, achievement of the target population coverage target and, in addition, access to diagnosis and treatment must be ensured by monitoring and managing the actions employed[19]. According to European recommendations, to achieve this success, at least 95% of these women need to be covered by the target population, at least 70% (85% desirable) and a participation rate of at least 70% (85% is desirable)[20].

In this study, it was observed that the epidemiological profile and survival of women with cervical cancer, inserted in the HRC under study, is consistent with what is described in the literature. However, a retrospective database study has limitations, such as selection bias, inclusion of patients, for analysis and possible loss of information during follow-up.

## CONCLUSION

This study showed that, even with cervical cancer prevention and early screening programs available in the health network, the diagnosis at an advanced stage persists, decreasing survival and causing the death of hundreds of women. The level of education proved to be the main factor for cervical cancer, since the higher the level of information and clarification, the less exposed women become to risk factors. Early-stage diagnosis provides longer survival; consequently, fewer women die from this cancer, which was observed in this study.

Given this, it is evident the need for quality evaluation and management of cervical cancer screening program and public policies related to this issue, as it is evident the difficulty for early diagnosis of this cancer, compromising the possibility of cure of affected women.

Future studies should evaluate adherence to cervical cancer screening programs, the quality of care provided and accessibility to the health system, as well as to evaluate diagnostic and therapeutic advances, as well as comparisons between public services and supplementary health in the care of these women.

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