EPIDEMIOLOGY OF CERVIX CANCER IN BRAZIL (2005-2015): STUDY OF MORTALITY AND HOSPITAL INTERVENTION RATES

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Abstract: Cervical neoplasia has high morbidity and mortality and is the main female gynecological neoplasia, but it is susceptible to early detection and cure. A major challenge for developing countries such as Brazil is the expansion of prevention programs, which becomes more effective when the epidemiology is known. The objective of this study was to conduct an epidemiological survey to evaluate the Brazilian panorama of this neoplasm. A temporal aggregate study was performed using the mortality and hospital admission rates for cervical neoplasia throughout the Brazilian territory during the years 2005 to 2015, data obtained through DATASUS and IBGE. During the years 2005 to 2015, there was a significant drop (p<0.05) in hospital admission rates in the 0-19, 20-39, 40-59, 60-79 years, with an average fall of 36 % and a death increase in the age group 20-39 years. The North region had a significant increase in death in the range ≥ 80 years, 140%, p<0.02. The mean mortality rate in Brazil was 5.14, with a 95% CI of 5.01 to 5.27. Cervical neoplasia is still present in Brazil, although mortality has a tendency to decrease, this tendency is unequally distributed in Brazil, with the north and northeast regions showing the highest rates. Better public policies are fundamental.

Keywords: Epidemiology. Uterine Cervical Cancer. Mortality. Hospitalization. Brazil.
1 INTRODUCTION

There are five types of female gynecological cancer, endometrial cancer, ovary, cervical cancer, vaginal and vulvar cancer. Studies show that one in five women has her gynecological cancer associated with sexual promiscuity and that 40% of women have a greater stigma involving gynecological cancer than other forms of the disease. Cervical cancer is the third most common tumor among women is already the fourth leading cause of cancer death in Brazil. In 99% of cases, the disease is related to the HPV virus. Ovarian cancer is less frequent and more difficult to diagnose, the disease does not present specific symptoms in its initial phase. In 75% of cases, most malignant tumors of the ovary manifest only at an advanced stage. Quite rarely, cancer of the vagina accounts for only 1% of gynecological tumors. While vulvar cancer, a disease that affects a woman’s external genital organ, is more common among postmenopausal women, but can also affect younger women. Sores or wounds that do not heal, do not fade and increase over time can be signs of illness.1,2

Cervical cancer is the most frequent neoplasm of the female genital tract, with an incidence of 17.8 cases per 100,000 women corresponding to 12% of all female cancers.3 This neoplasm becomes even more problematic and relevant in underdeveloped countries where data show annually an estimated 493,000 new cases and 273,500 deaths. Undoubtedly, cervical cancer is a serious public health problem with a high degree of morbidity and mortality in the female population.4,5

Cervical neoplasia represents a group of invasive disorders that present several subtypes, but the glandular (adenocarcinoma) and epithelial (squamous) variants represent 70 and 25% of the cases, respectively. Its growth is generally asymptomatic and there may be symptoms such as irregular bleeding, excessive bleeding and/or visible damage to the cervix.2,6,7

Human papillomavirus (HPV) infection is the main condition associated with the appearance of this neoplasm due to its malignancy.2,8,9 HPV is a DNA virus that presents more than 150 subtypes and is considered the etiologic agent of cervical cancer because it is in 99.7% of all cases, however, variants 16 and 18 represent 70% of that amount.2 Approximately 291 million women worldwide are carriers of HPV, 32% of whom are infected with HPV types 16, 18 or both. Comparing this data with the annual incidence
of approximately 500,000 cases of cervical cancer, it is concluded that cancer is a rare outcome, even in the presence of HPV infection. That is, HPV infection is a necessary but not sufficient factor for the development of cervical cancer. Factors related to immunity, genetics and sexual behavior appear to influence the still uncertain mechanisms that determine the regression or persistence of HPV infection and also the progression to precursor lesions or cancer. Thus, smoking, early sexual initiation, high number of sexual partners and pregnancies, contraceptive pill use and immunosuppression (caused by HIV infection or use of immunosuppressants) are considered risk factors for development of cervical cancer. Age also interferes with this process, with the majority of HPV infections in women less than 30 years old regressing spontaneously, whereas above that age persistence is more frequent.6,10

Studies have shown that cervical cancer is more frequent in countries with a poor and precarious triage.2,7 Underdeveloped countries in Latin America, the Caribbean, and Africa are the main bearers of this neoplasm, and this scenario is explained by the fact that only 5% of women in these countries have undergone screening in the last five years.2,11-13 In the meantime, developed countries that have a frequent practice of the Pap smear and use of vaccination against the HPV virus present lower rates of this pathology. These two measures have helped reduce the number of cervical cancer in developed countries by 75% in the last 50 years, and today, as in the United States, there are only 4,000 annually deaths from cervical cancer.2

In addition to HPV infection, other factors such as early sexual activity, multiple partners, high-risk partner, history of a sexually transmitted disease, immunosuppression, contraceptive use, low socioeconomic status, and smoking are risk factors associated with oncogenesis of this tumor. It should be noted that all of these factors are changeable, as a consequence, they are susceptible to intervention measures and, therefore, professionals and health agencies have an important orientation role in preventing this condition.1,2,9,14

The knowledge of the epidemiology of this tumor is one important and fundamental point for the planning of objective actions for the reduction of morbidity and mortality rates from this disease. Programs such as “Viva Mulher”, implemented in 2007, provide data on cervical cancer screening in Brazil and prove that there is a failure to cover the Pap test in the female population of the 20-year age group since only 8% perform the routine
examination. However, even with problems, the program was able to reduce mortality rates in the 50-59 age group.\textsuperscript{15-18}

Based on these premises, this study aimed to perform a retrospective analytical survey through a study of the database of the Sistema Único de Saúde (Unified Health System) (DataSUS), considering data on mortality and hospitalization to map the invasive cervical neoplasia in Brazil from 2005 to 2015. These epidemiological data allow us to know the reality of this pathology from the North to the South of the country and may foment future plans for the prevention, diagnostic and therapeutic intervention of cervical cancer.

2 METHODOLOGY

A retrospective study of temporal series aggregates with a quantitative exploratory and documentary approach was carried out. Data were collected from the Information and IT Department of the SUS (DATASUS, http://www.datasus.gov.br) of the Sistema de Informações sobre Mortalidade and of the Sistema de Informações de Morbidade Hospitalar (Mortality Information System and the Hospital Morbidity Information System), both by residence, in a period of 10 years (2005 to 2015) of all the states, dispensing the need to send to the Ethics Committee. Information was collected on the total number of deaths and hospital admissions for malignant neoplasms of the uterine cervix, CID-10 C53 specifically, not being considered the presence of metastasis as a factor of mortality, stratified by region and age (0 to 19 years, 20 to 39 years, 40 to 59 years, 60 to 79 years and equal to or above 80 years). Demographic data for each year and for each age group were obtained from IBGE (Brazilian Institute of Geography and Statistics) (IBGE, www.ibge.gov.br).

In the study, all deaths of women who had as their underlying cause the cervical cancer death were included based on the International Classification of Diseases (ICD): ICD-10 Diagnosis Code C53, Chapter II: Neoplasms (tumors). The gross rates of cervical cancer mortality adjusted by age group and region were calculated per 100.000 women. The average annual rates for the 10-year period were calculated, the time variable being represented in a decade.

The data were collected in January and February of 2018, using the DATSUS code ICD10, correlating with age, regions and proportion of feminine population of each variable.
The data were plotted statistically and analyzed quantitatively in the programs Microsoft Excel 2010 (Microsoft Corp., United States) and SPSS 12.0 (SPSS Inc., Chicago, United States). Statistical comparisons among the years were made by Student’s t-test for the parametric variables and Mann-Whitney for the non-parametric variables. The data were also treated in descriptive ways. The results were presented through graphs and tables for better interpretation and exposure. Values of $p \leq 0.05$ were considered significant.

3 RESULTS

From 2005 to 2015, there were 55,761 deaths and 264,733 hospital admissions throughout Brazil due to invasive cervical neoplasia. The general mortality rates for Brazil with population correction were 5.14 deaths per 100,000 inhabitants with a confidence interval (95% CI of 5.01-5.27) and the hospital admission rate was 24.41/100,000 (95% CI of 22.17-26.64), as shown in figure 1.
38.77/100,000 (95% CI of 31.55 -6), followed by the Midwest with 23.98/100,000 (95% CI of 21.71-26.24), Northeast with 23.4/100,000 (95% CI of 21.55-24.22), Southeast with 21.82/100,000 (95% CI of 20.28-23.36) and North with 16.2/100,000 (95% CI of 15.08-17.32). The North region presented the highest mortality rate with 7.61/100,000 deaths (95% CI of 6.96-8.27), followed by the Northeast region with 5.68/100,000 (95% CI of 5.55-5.99), Midwest with 5.49/100,000 (95% CI of 5.29-5.68), South with 5.11/100,000 (95% CI of 4.99-5.23) and Southeast with 4.27/100,000 (95% CI of 4.21-4.32).

Figure 2A – Mortality Rate and Hospital Hospitalization for Cervical Cancer in Southern Brazil (2005-2015).
Source: Datasus.
Note: Data were expressed per 100,000 inhabitants and categorized by age group.
Figure 2B – Mortality Rate and Hospital Hospitalization for Cervical Cancer in the Center-West Region of Brazil (2005-2015)
Source: Datasus.
Note: Data were expressed per 100,000 inhabitants and categorized by age group.

Figure 2C – Mortality Rate and Hospital Hospitalization for Cervical Cancer in the Northeast Region of Brazil (2005-2015)
Source: Datasus.
Note: Data were expressed per 100,000 inhabitants and categorized by age group.
Table 4 - Mortality Rate and Hospital Hospitalization for Cervical Cancer in the Southeastern Region of Brazil (2005-2015)

Note: Data were expressed per 100,000 inhabitants and categorized by age group.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Mortality rate</th>
<th>Hospital admission rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-19 years</td>
<td>0.01</td>
<td>0.19</td>
</tr>
<tr>
<td>20-39 years</td>
<td>1.39</td>
<td>13.77</td>
</tr>
<tr>
<td>40-59 years</td>
<td>22.46</td>
<td>49.52</td>
</tr>
<tr>
<td>60-79 years</td>
<td>39.89</td>
<td>49.66</td>
</tr>
<tr>
<td>80+ years</td>
<td>69.4</td>
<td>37.02</td>
</tr>
</tbody>
</table>

Figure 2D – Mortality Rate and Hospital Hospitalization for Cervical Cancer in the Southeastern Region of Brazil (2005-2015)

Note: Data were expressed per 100,000 inhabitants and categorized by age group.

Figure 2E – Mortality Rate and Hospital Hospitalization for Cervical Cancer in the Northern Region of Brazil (2005-2015)

Source: Datasus.
Note: Data were expressed per 100,000 inhabitants and categorized by age group.
There was a trend of increased mortality rates in the older age groups with a rate of 80 years old or more with a mean death rate of 27.33/100.000 (95% CI of 26.43–28.23), while the age group from 40 to 59 years old had the highest hospital admission rates (56.57/100.000) (95% CI 48.49–64.65).

When comparing the year 2005 to 2015, beginning and end of this study, it evidenced an increase in the total mortality rate in Brazil in 14% (0.05), followed by an increase in mortality in the 20–39 age group in 31% (p = 0.009). Almost all age groups showed a decrease in hospital admission rates, 60, 35, 51 and 31%, respectively for the age groups 0 to 19 years, 20 to 39 years, 40 to 59 years and 60 to 79 years, presenting a total reduction of 36% (0.05).

In the analyzes by region, it was verified that in the South there was a significant decrease of 20% mortality in the age range from 40 to 59 years. In hospitalization rates, there was a significant decrease in all age groups, except in the range of 80 years or above, with the overall rate falling from 62.2/100.000 to 25.5/100.000, a decrease of 59% (0.05).

In the Southeast, there was a significant decrease in the hospital admission rate in the age groups 0–19 years, 40–59 years and above or equal to 80 years. In the Midwest, there was a significant decrease in the hospitalization rates of the age groups from 0 to 19 years, 40 to 59 years, respectively, of 67 and 47%. In the North, there was an increase in mortality in the total rate and the age group of 20–49 years of 52 and 24% respectively (p 0.05). A 135% increase in mortality in the age group of 80 years or older p 0.02. In the Northeast, there was a decrease in the total hospitalization rates, such as in the age groups of 20 to 39 years, from 40 to 59 years.

Analyzing the proportion of deaths due to hospitalization, Brazil had an overall average of 21.06%. The region with the lowest rate was the South with 13.18% and the highest rate occurred in the North with 47%.

4 DISCUSSION

Brazil presents a very peculiar cervical cancer epidemiology, which can be considered intermediary among developed and underdeveloped countries. Data from
the country showed a mortality rate of 5.14/100,000 inhabitants, while developed countries such as the United States and Japan have rates ranging from 1.0 to 1.5/100,000, however, our data are below underdeveloped countries with an average mortality rate of 9.8/100,000.2,18,19

In the historical series studied, it was analyzed that in Brazil, during 10 years, there was a 36% drop (p < 0.001) in the rate of hospital admissions for this pathology. These data may be the result of expanding the opportunity to screening and campaigns and educational awareness measures to validate prevention and diagnosis.2,14,16,18

Data concerning the mortality from this cancer in younger women is alarming. One hypothesis for increased mortality in younger age groups such as 20-39 years would be the current female sexual behavior.

Girls are starting their sex life increasingly younger, in many cases still immature, unprepared and disoriented, being a risk factor for the development of cervical cancer, since they were exposed to very young people with HPV and other viruses.7,9 However, it is believed that this factor will decrease in the coming years, because in 2014, the Ministry of Health, through the National Immunization Program, began the campaign of vaccination of girls between 11 and 13 years against the HPV virus. The vaccine is the quadrivalent, which offers protection against HPV subtypes 6, 11, 16 and 18, this vaccine will make an important contribution to the actions of prevention of this cancer.20

According to a systematic review of the determinants of cervical cancer and coverage of Pap smears in Brazil, failure to perform the test is associated with low or high age, low level of education, low socioeconomic level, low family income, absence of gynecological problems, embarrassment or fear in relation to the examination, no medical consultation in the year prior to the survey, difficulty in accessing medical care, absence of medical request and non breast self-examination in the year prior to the survey.21

The overall mortality rates for cervical neoplasia by region tend to be dependent on the HDI (Human Development Index) of each respective region.14,15,17,18,22 Regions such as South and Southwest, with better HDIs, 0.749 and 0.7505 respectively, have the lowest mortality rates in the country, the Southeast with 4.27/100,000 (95% CI, 4.21-4.32) and the South with 5.11/100,000 (95% CI 4.99-5.23).Meanwhile, regions with worse HDIs
such as the Northeast and North presented the highest mortality rates, with the North region having the highest rate, 7.61/100,000 deaths (95% CI 6.96-8.27) and Northeast with 5.68 / 100,000 (95% CI of 5.55-5.99). However, a very peculiar contradiction is that these two regions do not present the highest hospitalization rates, a factor that could explain the reason for the higher mortality. For instance, the North region presented the highest mortality rates and the lowest hospital admission rates, this is an important point of this study since it shows that public health activities aiming at active case search, diagnosis, adequate treatment and especially preventive measures should be expanded in this region. It corroborates the lack or lack of preventive action measures in these regions, aspects of sexual behavior, such as the early age of first sexual intercourse and multiple partners, factors that increase the risk of contracting HPV and make these regions the most urgent places for measures of prevention.24,23

Another important finding observed in this study was an increase in the rate of hospitalization in the age group from 40 to 59 years. It is believed that the highest incidence of hospitalization in the age group from 40 to 59 years is because this age group constitutes one of the main target populations of the programs of prevention of cancer, having a greater prevalence of diagnosis. In addition, the early onset of sexual life, multiplicity of sexual partners, inadequate intimate hygiene, HPV infection in adolescence; prolonged use of oral contraceptives; smoking are cumulative factors that will contribute to the expression of this neoplasm later.

Based on the high mortality rates in the age range ≥ 80 years in the North region, at 69.40 / 100,000, there was an increase of 150% above the national average for the same age group. In addition, it increased significantly by 140% in mortality when compared to the years 2005 to 2015, and mortality rates in states such as Amapá, Roraima, Amazonas reached, respectively, 230, 217, 176/100,000 for this age group. These worrying data make it clear that it is necessary to rethink the cervical cancer screening approaches being addressed in this region, and an eminent effort must be made to contain these alarming data.

It is notable that the sexual behavior of the older age groups has changed. An increase in the number of sexual partners and sexual relations, often unprotected, may contribute to the increase of the neoplasia in this group.24,25 It is also important to mention that cervical cancer is a slow-developing disease that can progress without early-onset
symptoms and develop into symptoms with often nonspecific symptoms such as intermittent or postpartum vaginal bleeding and abdominal pain associated with urinary complaints or intestinal disorders in the most advanced cases. Another important factor that corroborates this epidemiology is the fact that screening with routine exams such as Pap smears is discontinued after 65 years old, before these data, it is suggested to increase the age of the screening tests for populations at risk, especially in the North.

Still, in the North region, it is worth mentioning the high amount of deaths due to hospitalization. Compared with the value found for Brazil (21.06%), the values found in this region exceed the national average by more than 25%.

Despite the updated publication of the Brazilian Guidelines for the Screening of Cervical Cancer by INCA in 2014, from the institution of Ordinances as 189/2014 that established the Reference Service for Diagnosis and Treatment of Precursor Injuries of Cervical Cancer, the National Qualification in Cytopathology in the prevention of cervical cancer (QualiCito) redefined by the Ministry of Health’s Resolution 3,388 / 2013 and the National Immunization Program, it is noticed that in some states, especially in the northern region of the country, the tragic scenario remains evidencing that malignant neoplasm of the cervix is still a challenging situation for the national context. Even though there are several risk factors, the vast majority of them are changeable, controllable and preventable, such as permanent HPV infection, mainly from high-grade strains such as 16 and 18, early sexual initiation, multiple partners and smoking, which makes this disease decrease its incidence and mortality. However, as their oncogenesis period is long, the results of screening and vaccination campaigns will not be perceived rapidly. Only in a few years will there be significant reductions in hospitalization and mortality due to this neoplasm due to vaccination.

5 CONCLUSION

Malignant neoplasm of the cervix is a frequent disease associated with high morbidity and mortality in the female population. It represents a pathology with important epidemiological relevance that deserves special attention from society, the medical community and government. Once the disease is diagnosed in the early stages, it has
a good prognosis and a minimally invasive treatment, which is why screening for this disease is essential. The data in the present study show that the South and Southeast regions suffered a reduction in mortality rates due to the pathology. However, the Northeast region and, in particular, the North region of the country present the most tragic outcomes, morbidity and mortality rates, and the lowest rates of admissions. Efforts should be redirected to this region to guide preventive actions by the public health system, highlighting their frequency and associated risk factors.

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CONTRIBUTORS

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