doi: http://dx.doi.org/10.11606/issn.1679-9836.v104i2e-227046 Rev Med (São Paulo). 2025 Mar-Abr;104(2):e-227046.

Article

Cervical Cancer Mortality in Alagoas between years 2001 to 2019: An Ecological Study

Mortalidade por câncer de colo de útero em Alagoas entre os anos 2001 a 2019: um estudo ecológico

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Silva JPM, Barboza TDT, Tomé TKBV. Cervical Cancer Mortality in Alagoas between years 2001 to 2019: An Ecological Study / *Mortalidade por câncer de colo de útero em Alagoas entre os anos 2001 a 2019: um estudo ecológico.* Rev Med (São Paulo). 2025 Mar-Abr;104(2):e-227046.

ABSTRACTS: Introduction: Cervical cancer (CC) is a largely preventable neoplasm that still has a high incidence and mortality rate in the Brazilian female population. **Objective**: This study aims to investigate the epidemiological profile, trends and spatial distribution of CC in the state of Alagoas from 2001 to 2019. **Methods**: This is an ecological study that includes female deaths caused by CC in the period from 2001 to 2019 in the state of Alagoas, Brazil. The following sociodemographic variables were used: age group, race/ethnicity, marital status, and education. Mortality analysis was performed using the joinpoint regression model. The Moran's index was calculated for spatial analysis. Vaccine coverage was assessed using administrative methods. **Results**: Regarding mortality, the following observations were made: i) an increase in cervical cancer mortality between ages 20 and 29; ii) 70.3% of deaths occurred in the 25 to 64 age group; iii) individuals of mixed race had the highest percentage of deaths at 57.75%; iv) a reduction in the risk of death with increased education; v) a decrease in mortality rate with improved socioeconomic conditions. Additionally, there was a decline in vaccine adherence. **Conclusion**: The state of Alagoas experienced an increase in CC mortality between 2001 and 2019. Furthermore, there was a decrease in vaccine adherence. Therefore, we emphasize the importance of screening for prevention and the need for an expanded *Human Papillomavirus* (HPV) vaccination campaign.

KEY WORDS: Cervical Neoplasms; Mortality; Women's Health; HPV.

RESUMO: Introdução: O câncer de colo de útero (CCU) é uma neoplasia, na maioria dos casos, prevenível que ainda tem uma alta incidência e mortalidade na população feminina brasileira. Objetivo: Este estudo tem por objetivo principal investigar o perfil epidemiológico, tendência e distribuição espacial da mortalidade por CCU no estado de Alagoas no período de 2001-2019. Métodos: Trata-se de um estudo ecológico. Incluirá os óbitos femininos causados por CCU no período de 2001 a 2019 no estado de Alagoas, Brasil. Foram utilizadas as seguintes variáveis sociodemográficas: faixa etária, cor/raça, estado civil e escolaridade. A análise da mortalidade foi feita a partir do modelo de regressão *joinpoint*. Foi realizado o cálculo do índice de Moran para a análise espacial. A cobertura vacinal foi feita utilizando o método administrativo. Resultados: Quanto a mortalidade, observou-se: i) crescimento da mortalidade por CCU entre 20 e 29 anos; ii) 70,3% das mortes ocorreram na faixa entre 25 e 64 anos; iii) a cor parda obteve o maior percentual de mortes com 57,75%; iv) Redução do risco de morte com o aumento da escolaridade; v) redução da taxa de mortalidade com a melhora nas condições socioeconômicas. Também verificou-se uma queda na adesão à vacinação. Conclusão: O estado de Alagoas apresentou aumento na mortalidade por CCU no período entre 2001 e 2019. Além disso, houve redução na adesão à vacinação. Portanto, destacamos a importância da triagem na prevenção e a necessidade de ampliação da campanha de vacinação contra o *Papilomavírus Humano* (HPV).

PALAVRAS-CHAVE: Neoplasia Intraepitelial de Colo Uterino; Mortalidade; Saúde da mulher; HPV.

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INTRODUCTION

Cervical cancer (CC), excluding non-melanoma skin tumors, is the third most common cancer among women in Brazil[15]. In 2019, the age-adjusted incidence rate in the country was 15.38 per 100,000 women, and the mortality rate was 5.33 deaths per 100,000[16]. Regionally, the North had the highest mortality rate during the same period, with 12.58 deaths per 100,000 women, followed by the Northeast, Central-West, South, and Southeast, with rates of 6.66, 6.32, 4.99, and 3.71, respectively[16]. The disease has two main histological types: squamous cell carcinoma (80% of cases) and adenocarcinoma (including adenosquamous carcinoma), accounting for 10–15% of cases[27].

Persistent infection by the human papilloma virus (HPV) is the main risk factor associated with the development of the neoplasm. In turn, a high number of sexual partners, a young age in the first sexual intercourse, increasing parity, immunosuppression, human immunodeficiency virus infection and smoking are cofactors that contribute to the natural history of the disease, whether facilitating HPV infection, favoring persistent infection or leading to the progression of precursor to invasive[32] lesions.

HPVs are small double-stranded DNA viruses belonging to the Papillomaviridae[25] family. Currently, over 200 types of HPV are known, of which 15 (e.g., types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82) are considered high-risk types due to their association with carcinogenesis. Among these, HPV 16 is the most prevalent in cervical diseases, followed by HPV 18[37],[30].These viruses are also linked to lesions on the feet, genital and hand warts, squamous cell carcinomas of the head and neck, esophageal cancer, and brain and lung tumors[25].

The integration of high-risk HPV into the host genome during persistent infections is believed to be the main molecular event in cervical carcinogenesis. The subsequent expression of oncoproteins E6 and E7, interfering with a variety of key cell molecules, including the inactivation of tumor suppressor genes p53 and retinoblastoma protein (pRB), respectively, are the main contributors to the malignant transformation of the cervix[37].

Cervical cancer is a preventable and successfully treatable cancer, as long as it is detected early[35]. In this sense, in August 2020, the World Health Assembly adopted the Global Strategy for the elimination of the disease. To achieve this goal, three main pillars must be observed: vaccination, screening and treatment. The proposed goals to be achieved by 2030 are: 90% of girls fully vaccinated against HPV by the age of 15, obtaining 70% of women screened using a high-performance test at age 35 and again at age 45 and a proportion of 90% of women with pre-cancer and invasive cancer treated [36].

In Brazil, several actions, therefore, can be cited.In 2014, the quadrivalent vaccine against HPV 6, 11,16 and 18, from Merck Sharp & Dohme (trade name Gardasil), was then introduced into the National Immunization Program. The target audience is currently girls from 9 to 14 years old, boys from 11 to 14 years old and people from 9 to 29 years old living with HIV/AIDS, in addition to individuals undergoing solid organ/bone marrow transplants and cancer[13] patients. In 2021, immunosuppressed women aged 26 to 45 were also included [3]. For cervical cancer screening, the cytopathological examination is indicated for women between 25 and 64 years old and who have already had sexual activity, and repetition is recommended every three years, after two consecutive normal examinations performed with an interval of one year[12].Women diagnosed with intraepithelial lesions of the uterine cervix are then referred to secondary care for diagnostic confirmation and treatment, according to established[12] clinical guidelines. It also highlighted the goal established, through the most recent Strategic Action Plan for Confronting Chronic Diseases and Non-Communicable Diseases, of reducing premature mortality (30 to 69 years old) from cervical cancer by 20%, in the country, by 2030[14].

Despite the efforts, cervical cancer is still a relevant public health problem, with remarkable disparities in incidence and mortality between Brazilian regions. In this perspective, the knowledge of the profile of morbidity and mortality from cervical cancer, within each reality of the Brazilian states, is essential for the effective direction of health actions that promote the prevention and early diagnosis of this population in order to reduce complications inherent in late diagnosis, increase the chances of cure and survival of these patients, as well as reduce mortality rates.

The main objective of the study is to investigate the temporal evolution of the cervical cancer mortality rate in the state of Alagoas in the period between 2001 and 2019.

OBJECTIVES

Primary Objective

a.To investigate the trend, epidemiological profile, and spatial distribution of cervical cancer mortality in the state of Alagoas between 2001 and 2019.

Secondary Objectives

a.To describe the cervical cancer mortality rate during the analyzed period;

b.To assess the mortality trend based on socioeconomic parameters: race/ethnicity, age group, and educational level in the state of Alagoas;
c.To evaluate HPV vaccination coverage in the state.

METHODS

Type of Study

This is an ecological, quantitative study based on the analysis of secondary public-domain data from health information systems and other governmental databases.

Data Sources

All data were collected between 2022 and 2023 from

TabNet, a tool provided by DATASUS to generate tables, graphs, and maps. Data were extracted from the following systems: i) Mortality Information System (SIM); ii) Resident Population estimates; iii) National Immunization Program Information System (SI-PNI).The extracted data were stored in *Google Sheets* to facilitate handling.

Variables Analyzed

SIM data were obtained using the following criteria: i) Available periods: 2001–2019; ii) State: Alagoas ;iii) ICD-10 category: C53 – Malignant neoplasm of the cervix uteri.The analyzed variables included: age group, race, education level, marital status, place of occurrence, and municipality.

Population estimates used to calculate mortality rates were selected with these criteria: i) State: Alagoas; ii) Period: 2001–2019; iii) Sex: female; iv) Resident population by age group 1.

The age group classification used for both death and population data was: under 20, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and 80 years or older.

In turn, to obtain the population estimate data used in the calculation of vaccination coverage, two searches were made. In the first search, the criteria used were: i) Federation Unit: Alagoas. ii) Period 2014-2019; iii) Gender: Female; iv) Simple age: 9-13 years. And for the second search, the criteria were: i) Federation Unit: Alagoas; ii) Period 2014-2019; iii) Gender: Male; iv) Simple age: 11-14 years.

Finally, the data on vaccination were also extracted from TABNET using the SI-PNI data, with the following criteria: i) Period: 2014-2019; ii) Federation Unit: Alagoas; iii) Immunobiological: Quadrivalent HPV - Female; Quadrivalent HPV - Male; iv) Doses: 1º dose; 2º dose.

TIME FRAME ANALYZED

Mortality data were obtained using the period between 2001 and 2019 in Alagoas. Exceptionally, as the HPV vaccine was introduced into the vaccination schedule only in 2014, vaccination data were collected between 2014 and 2019.

For statistical purposes, the population used in the period corresponded to the relative to the data obtained, that is, for mortality the period between 2001 and 2019 was used and for vaccination 2014 and 2019.

STRATEGY FOR DATA ANALYSIS

STRATEGY FOR MORTALITY RATE ANALYSIS

The analysis of the mortality rate was carried out in three stages:

A) In the first stage, the descriptive analysis (absolute and relative frequencies) was performed. To calculate the mortality rate, the following equations were used:

I) Annual mortality rate of the State

$$Rate = \frac{Numbers\ of\ deaths\ from\ CC\ in\ the\ period}{Female\ population\ in\ the\ period}\ x\ 100.000$$

Ii) Mortality rate by municipality

$$Rate = \frac{Numbers\ of\ deaths\ from\ CC\ in\ the\ local\ (2001-2019)}{Female\ population\ in\ the\ local\ (2001-2019)}\ x\ 100.000$$

$$Rate = \frac{Numbers\ of\ deaths\ from\ CC\ in\ the\ local\ (2001-2019)}{Female\ population\ in\ the\ local\ (2001-2019)}\ x\ 100.000$$

B) In the second part, the *joinpoint* regression model was used. It was chosen because it allows you to analyze temporal trends by checking if this trend is better explained in line segments (*joinpoints*) than in a single line. In addition, it defines the APC (*Annual Percent Change*) which is calculated to describe the trend and significance[1]. Thus, APC > 0 indicates that rates are increasing, APC < 0 indicates that they are decreasing and APC = 0 are neither increasing nor decreasing7.

C) Finally, for a better understanding of the data, the spatial analysis of the mortality rate by municipality was made. For this purpose, the *Moran* index (I) was calculated. This calculation results in a number that defines the dependency relationship between polygons. For this, it is considered that there is direct dependence when [I > 0], inverse dependence when [I < 0] and there is no dependence (null hypothesis) when [I = 0]. In addition to the index, the pseudo-significance value (p-value) is also calculated, which indicates the degree of confidence of this index. The Moran index is considered reliable when [p-value ≤ 0.05] because it indicates that the confidence is at least 95%. Therefore, if [p-value > 0.05] indicates that confidence is low and, consequently, disregards the spatial correlation19. Following this reasoning, the *TerraView* 5.6.4 software was used to calculate the Moran index. Also, the *QGIS Desktop* 3.28.2 software was used to create the maps.

STRATEGY FOR VACCINATION COVERAGE ANALYSIS

The calculation of vaccination coverage was made by the administrative method. This method consists of the division between the doses applied and the population studied, multiplied

by 100. Thus, the vaccinated[22] target population is obtained. It should be noted that for the calculation of the number of total doses applied, the sum of the number of 1º doses and 2º doses for each sex was made.

Vaccination rate calculation:

A) Annual female HPV vaccine coverage

B) Annual male HPV vaccine coverage

RESULTS

In the period studied, from 2001 to 2019, 1,638 deaths from cervical cancer were identified in the State of Alagoas.

Of these deaths, 0.12% in the age group between 15-29 years (n= 2), 3.23% between 20-29 years (n=53), 13.73% between 30-39 years (n=225), 23.32% between 40-49 years (n=382), 21.97% between 50-59 years (n=360), 17.58% between 60-69 years (n=288), 11.96% between 70-79 years (n=196) and 8.05% between 80 years or more (n=132).

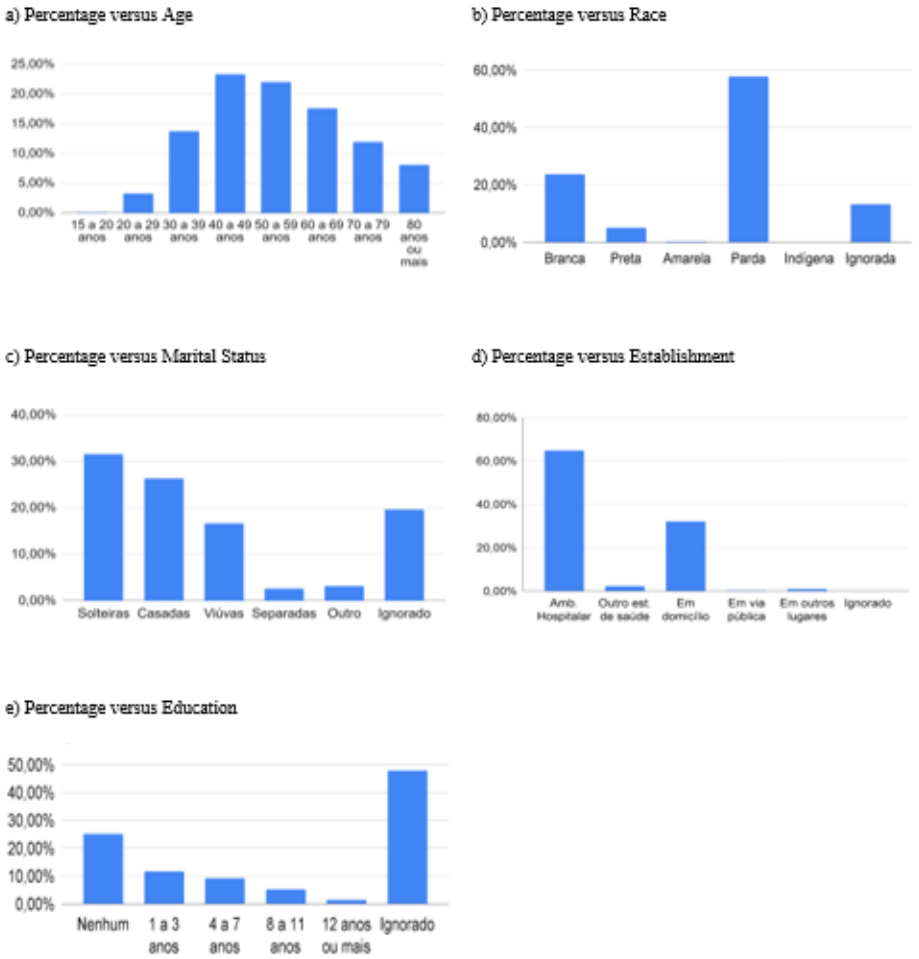
As for race, 23.74% (n=389) of the deaths were white, 4.94% (n=81) black, 0.24% (n=4) yellow, 57.75% (n=946) brown, 0.12% (n=2) indigenous and 13.18% (n=216) ignored. Regarding marital status, 31.56% (n=517) were single, 26.37% (n=432) were married, 16.66% (n=273) were widows, 2.62% (n=43) judicially separated, others (n=51) were notified in 3.11% of cases and ignored field corresponded to 19.65% (n=322) of the records. Regarding deaths, 64.71% (n= 1060) occurred in a hospital environment, 2.19% (n=36) in another health facility, 32.05% (n=525) at home, 0.12% (n=2) on public roads, 0.85% (n=14) in other places and 0.06% (n=1) of the cases were registered as an ignored place of occurrence.

In the field of study years, 24.96% (n=409) had no year of schooling, 11.47% (n=188) had 1-3 years, 9.15% (n=150) 4-7 years, 5.18% (n=85) 8-11 years, 1.46% (n=24) 12 years or more, however most, 47.74%, of the records had the field of study ignored.

The trend regression model showed a significant trend of growth in female mortality, considering the gross rate (APC=3.7, p<0.001), whose mortality went from 4.01/100 thousand in 2001 to 6.68/100 thousand in 2019. Highlight for age group 20-29 years (APC=6.9, p=0.0001), the other age groups showed stationary growth.

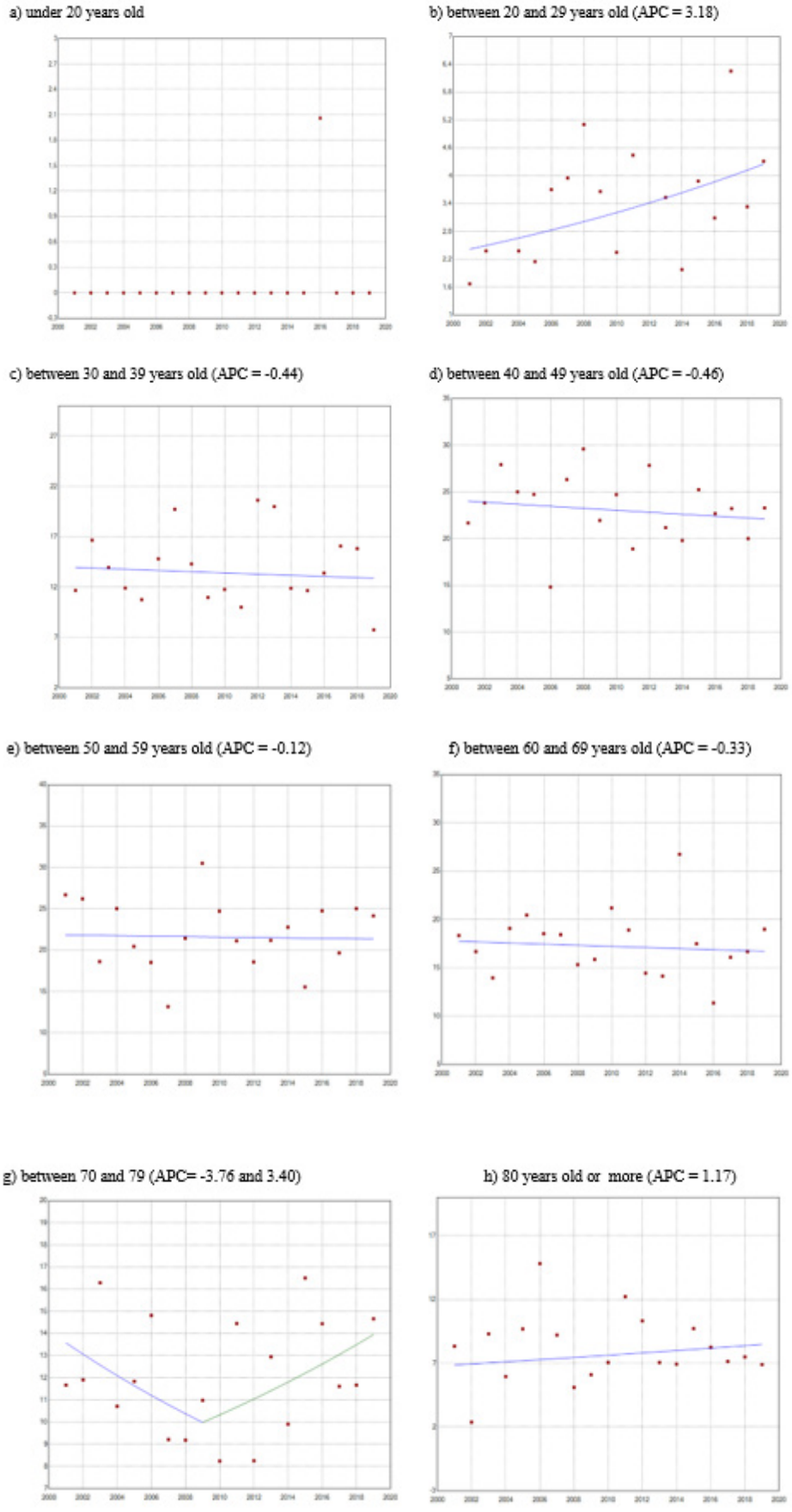
The mortality trend was stationary for all types of breed. The survey also showed a significant trend of mortality growth in the range of those with 4-7 years of study and decrease in those with 12 years or more, and in the other schooling groups (1-3 years of study and 8-11 years of study) the trend was stationary.

FIGURE 1 - Cervical cancer mortality rate in the state of Alagoas, Brazil, between the years 2001-2019



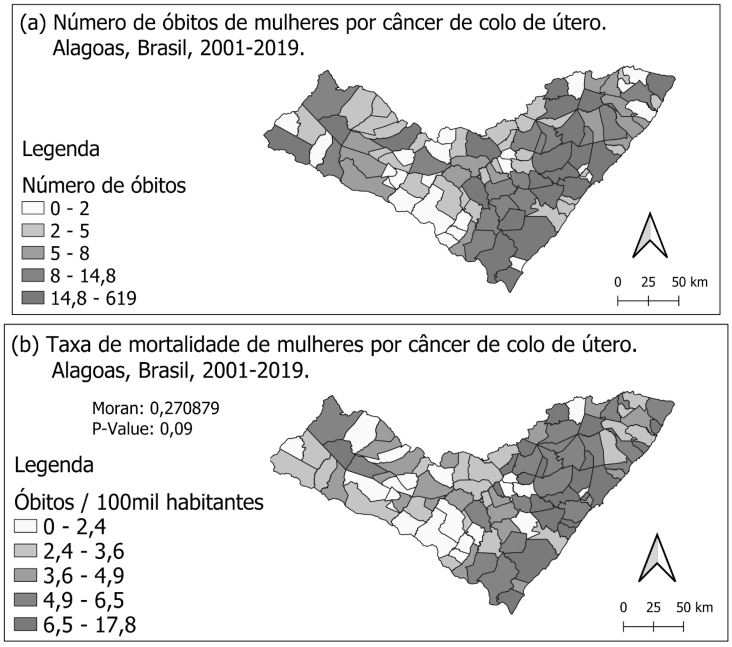
1 Sistema de Informação sobre Mortalidade
Source: MS. SUS SIM1 (2023)

FIGURE 2 - Trend of female mortality from cervical cancer according to age group in Alagoas, Brazil, 2001-2019



Source: MS. SUS. SIM[1] (2023)

FIGURE 3 - (a) Map with the number of deaths of women from cervical cancer in Alagoas, Brazil, in the period between 2001 and 2019; (b) Map with the mortality rate of women from CCU in Alagoas, Brazil, 2001-2019



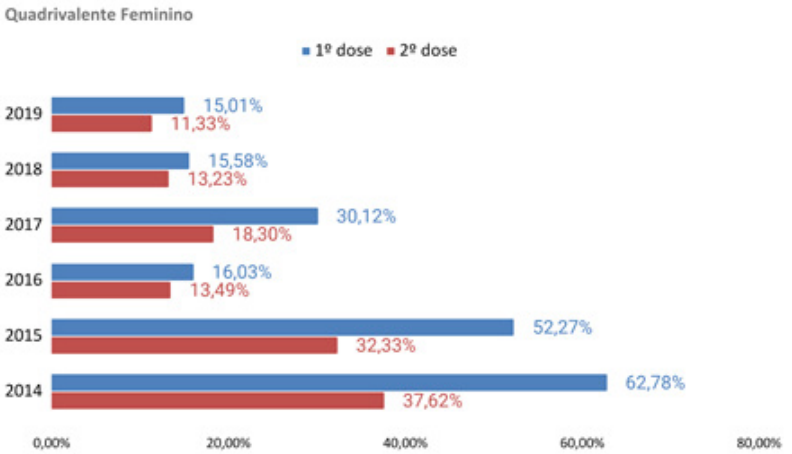
Source : MS. SUS. SIM[1] (2023).

In the spatial analysis, only two municipalities did not register deaths in the period, Belo Monte and Mar Vermelho, and two recorded more than 100 deaths, 110 in Arapiraca and 619 in Maceió. The highest mortality rates were from Pindoba (338.1/100 thousand), São José da Laje (228.8/100 thousand), Bélem (179.5/100 thousand), São Miguel do Milagres (173.3/100 thousand), Inhapi (171/100 thousand), Piaçabuçu (168.3/100 thousand), Roteiro (151.6/100 thousand), Joaquim Gomes (144.6/100 thousand), Rio Largo (144.1/100 thousand) and Chã Preta (139/100 thousand). The Moran Global statistic did not show significant spatial dependence (I=0.270879; p-value=0.09), which is why the Moran local statistic was not applied.

Regarding vaccination coverage, it is worth highlighting the variations in relation to the vaccination schedule and the target audience by period and their effects on adherence analysis depending on the variables used for study. The quadrivalent vaccine introduced in 2014 had a three-dose vaccination schedule (0.6 and 60 months) and, as a target audience, girls aged 11 to 13 years. From 2015, vaccination was extended to girls aged 9-13 years and in 2017 to girls between 9-14 years old and boys aged 11-14 years, and in 2016 the scheme went to 2 doses (0 and 6 months). Within this period other groups, in addition to adolescents, were contemplated. Therefore, the clipping made in this study aimed to observe, above all, the fluctuation over the years of adherence to the complete vaccination schedule.

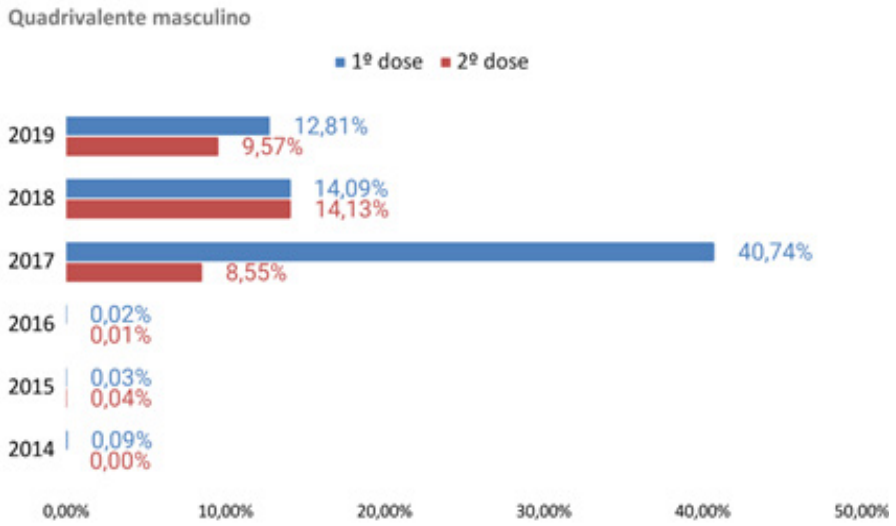
Below are the graphs related to vaccination coverage in Alagoas, in the period between 2014 and 2019, from girls between 9-13 years old and boys between 11 and 14 years old to the quadrivalent vaccine against the human papilloma virus.

FIGURE 4 - Distribution of the adherence rate to the 1º and 2º dose of HPV vaccination in the female population, in the State of Alagoas between 2014-2019



Source: MS. SUS. SIM[1] (2023)

FIGURE 5 - Distribution of the adherence rate to the 1º and 2º dose of HPV vaccination in the male population, in the State of Alagoas between 2014-2019



Source: MS. SUS. SIM[1] (2023)

DISCUSSION

The CC is the fourth leading cause of death in the female population from cancer in Brazil, being marked by a remarkable variation in health inequities among the units of the federação[11,20]. Thus, it is vehement importance of studies that allow the evaluation of the mortality trend for neoplasia, describe the socio demographic profile of the affected population, as well as point out the scope of prevention measures already implemented in a way circumscribed to each reality of the Brazilian states.

The analysis of time series, proposed by this work, allows, after analyzing the movement of measures of interest in health, to precede future scenarios of disease distribution in the population, conferring knowledge that allows to positively interfere in the ongoing processes[2]. It is therefore a salutary step for the coherent and based structuring of health planning and management measures aimed at improving the health levels of the population and improving the system.

In the present study, a significant growth trend in cervical cancer mortality was observed in the state of Alagoas, with emphasis on the age group of 20-29 years. Of a similar nature, a study that evaluated mortality in Brazil from CCU between the years 1996-2015 observed a growing trend of mortality in the country for women between 15 and 24 years, despite the stability observed between 25-64 years and 65 years or more, although with high rates. These findings were related to the available guidelines, with women outside the screening age group performing the preventive examination opportunistically, that is, when they seek care for other causes, despite the tenacity of the risk factors verified in this population[33].

In turn, the Moinho de Vento[3] Hospital Association, in a multicenter study to evaluate the national prevalence of HPV made with men and women between 16 and 25 years old, sexually active, not vaccinated against HPV, found a global prevalence of the virus of 53.6%, with 35.2% of these of at least one high-risk HPV for CC. The study also pointed out the persistence of other risk factors such as early age of onset of sexual activity, with an average of 15.2 years, with 49.9% of the women in the study having already been pregnant, with the average age for the first pregnancy of 17.3 years and, also, only about half of the individuals (50.7%) reporting the use of condom routinely and only 40.3% claiming to have used it in the last sexual intercourse. In addition, it is noteworthy that only 40.1% of the participants have already been informed about HPV by a health professional[3].

This information shows the lack of strengthening health education strategies, a lack that can lead to ignorance about the nosological entity in question and the consequent lack of taking the recommended prevention measures[17].

Therefore, this study found that 70.3% of deaths were within the target age group (25-64 years) of the screening programs, with 0.97% below and 28.8% above this. This finding can be justified, among other factors, by the time necessary from infection with the human papilloma virus for the development of cervical cancer, with a higher risk of progressing to death with advancing age, after 32.5 years, with the peak in older women[8].

All these factors added up, ratify the age group recommended for screening by the Ministry of Health. These also assert the urgency of articulated actions that ensure the access of population groups at risk to screening programs given the perpetuation of the growth of fatality of cases associated with this disease revealed in this study.

Another key aspect for understanding the mortality trend is its relationship, both with the prevalence of risk factors in the population, and with access to screening and timely treatment[20,21].

In this sense, it should be noted that the average mortality rate in Alagoas in the analyzed period was 5.23 deaths/100 thousand, with the two highest mortality rates, 6.95 and 6.68, observed in the last two years, 2018 and 2019, respectively. Simultaneously, the coverage of the main screening test provided

by the health system, the cytopathological, showed a decline in the state, especially in 2018 and 2019, with 3.6% and 3.27% of Alagoas women covered in this order, not reaching 10% of coverage since 201628. These local data are in tune with the low coverage of the screening throughout the country, with the north and northeast regions maintaining the lowest values, thus following, given the socioeconomic disparities between the Brazilian regions, the inverse relationship between the human development index and the CC reported in the literature[28].

Also, the difficulties in following up lesions suggestive of CC in Alagoas, an important factor for the early start of treatment and subsequent therapeutic results. This is because the continuity tests in the line of care given the suggestiveness of intraepithelial injury or cancer in the screening examination, namely, colposcopies and cervical biopsies, have been exhibiting a small scale in relation to the scale of cytopathological examinations performed in the state[30].

Nevertheless, it is worth emphasizing that CC mortality is considered avoidable since there are well-defined stages in the natural history of this disease. The implementation of screening plans with free access, high population coverage and follow-up guarantee in countries such as Canada, Scandinavian countries, England, South Korea and Singapore, promoted significant reductions in the incidence and mortality of the disease20. Therefore, it is necessary to promote an organized screening program, with prioritization of the active search of the population in the target age group, the inclusion of alternative screening tests, such as DNA-HPV, and adequate follow-up of women with altered results and/or confirmed diagnosis, as well as the adoption of evaluation mechanisms and continuous monitoring of actions aiming at the control of the disease in the state and consequent impact on the temporal trend of mortality[28].

In this study, the highest percentage of deaths was found in the brown color/race (57.75%). This result can be explained by the specific characteristics in relation to race and deaths from CC of each Brazilian region, with the North and Northeast regions presenting higher rates in brown women, in the Midwest Region in indigenous women and in the South and Southeast Regions in black women[8].

Another determinant of mortality refers to schooling. The higher the schooling, the lower the risk of CC. This is because a few years of study are considered a limiter of the understanding of the disease, which can lead to greater exposure to risk factors because they do not clearly understand how they increase the probability of illness10. It is important to note that 47.74% of the data recorded in Alagoas had the field of schooling "ignored", expressing a failure in the health surveillance system that makes it impossible to complete the analysis of the morbidity and mortality profile by CC in the state.

An additional point is the correlation, well reported in the literature, between sociodemographic indicators and CCU[10,20,21,26,28,31,33]. Rocha[26] (2017), points out that the improvement in socioeconomic conditions over time was accompanied by a statistically significant inverse association with CC mortality rates. It emphasizes that per capita household income remained significantly associated with lower mortality rates. It then suggests social investment, training to improve these indicators, as a possible way to address the death rates by CC. Another element pointed out is the relationship between infrastructure (funding) for Primary Health Care (PHC) and the reduction of these rates, emphasizing the role of PHC as a catalyst for screening procedures, increasing treatment possibilities and improving the quality of life of patients[26].

The state of Alagoas has 102 municipalities with a territorial extension of 27,767.66 km/2. Only the capital, Maceió, and Arapiraca with populations of 932,748 and 214,006 inhabitants, in sequence, showed more than 100 deaths throughout the time frame of the work, these being the most populous cities in the state according to the 2010 census. In this study, it was also observed that the municipalities with the highest mortality rates from CC, namely Pindoba, São José da Laje, Belém, São Miguel dos Milagres, Inhapi, Piaçabuçu and Roteiro expressed very low or low rates of municipal human development (MHMI), being from the highest death rate to the lowest, 0.574, 0.573, 0.593, 0.591, 0.484, 0.572, 0.505, respectively, according to Atlas-Brazil[4].

In turn, Soares[31], in a spatial analysis of Rio Grande do Norte, points out as the main result of his work the association found between higher rates of deaths from CC and low HDI/ precarious living conditions, indicating the difficulties of access of inland municipalities to the prevention, control and treatment of neoplasia as one of the elements that cooperated negatively for the increase of this indicator, thus corroborating the results found here.

Also, these are the findings regarding vaccination coverage in the state. Higher coverage values were observed in the year of introduction of the vaccine and a drop in the following years. These findings can be justified by the vaccination strategy in schools, both public and private, adopted in the year of insertion of the HPV vaccine in the adolescents' vaccination calendar, which allowed a nationwide coverage of 80% in just three months[29]. However, the psychogenic outbreak that occurred in Bertioga, municipality of São Paulo, associated with the HPV vaccine, which had wide media dissemination, possibly acted as the main factor in reducing the acceptance of the vaccine by the adolescent public[29].

In addition, other factors have been listed as central barriers to the achievement of vaccination goals against HPV in Brazil. The National School Survey, from 2019, in a study that evaluated the vaccination situation against HPV among adolescents aged 13 to 17 years, revealed that the most frequent reason for not vaccination was ignorance of the need to take the vaccine (public school:49.2%; private school: 31.4%), being the most frequent response in the states of the North and Northeast region, still corresponds to 62.9% of the responses among school children in Alagoas[29]. Other reasons pointed out, in smaller proportions, were the distance or difficulty to get to the unit or service, fear of reaction to the vaccine and non-authorization by those responsible[2].

It is also pertinent to emphasize the global phenomenon of vaccination hesitation. This is defined as the delay or refusal to vaccinate even when vaccines are available, a complex process with several causas[18]. Motivations for vaccination hesitation include distrust of health authorities, religious or

philosophical beliefs, fear of side effects and limited access to reliable information[5]. Given the urgency of the issue, the WHO recognized vaccination hesitation as one of the ten main threats to global health, and included the increase in vaccination coverage against HPV as the main strategy for the eradication of cervical cancer worldwide[34].

Misinformation about vaccines, amplified by social networks, has exacerbated this phenomenon. Studies show that fake news is one of the main causes of vaccination hesitation, with significant variations in hesitation rates between different countries[24]. Myths about side effects and the erroneous association of the HPV vaccine with the promotion of early sexual activity have contributed to low adherence to vaccination[6].

The ability to access, understand, evaluate and apply health-related information, known as health literacy, plays a fundamental role in the detection and mitigation of fake news[24], and should be encouraged and promoted by civil and health authorities. However, vaccination hesitation remains a global challenge, with significant implications for public health.

Our study also observed a considerable difference in adherence between boys and girls to the vaccine. Such an event may be linked to socially instituted differences regarding the naturalization of the responsibility of female adolescents for pregnancy, as well as the prevention of sexually transmitted diseases, including HPV[26]. An adequate approach to the sexual and reproductive rights of this population is therefore essential in order to highlight the role of everyone in the prevention of CC.

It is worth noting the limitation in the collection of data on HPV vaccination. This is due to the fact that the Information System of the National Immunization Program (SI-PNI) is still being implemented during the analysis period of this work[23].

Finally, I highlight the role of the health professional as a source of information on HPV. Kops17, 2019, in a cross-sectional, multicenter national study that included sexually active young people users of the public health system of the capitals of 26 states, concluded that the source of information associated with higher knowledge scores about HPV were the combination: health professionals and media. Another revealing fact of the study is that 75.91% of the respondents had knowledge about vaccination, however they did not know key points about the infection, especially regarding the link between sexual behavior and cancers related to HPV, being the variable education lower than the one that most interfered in this process.

It is therefore evident the importance of the direct action of health teams in the education of the population, promoting the transmission of adequate information that both sensitizes the target audience to the need to take the recommended prevention measures, as well as emphasizes the safety of immunobiologicals.

CONCLUSION

This study showed the epidemiological situation of the CC in the state of Alagoas, Brazil, in the period between 2001 and 2019. In it, it was found that there is a trend towards mortality growth, especially in the age group between 20 and 29 years. Still, it was observed that most deaths (70.3%) occur between 25 and 64 years old, which is an age group covered by screening programs. Finally, it was observed that the mortality rate in the analyzed period was 5.23 deaths/100 thousand inhabitants.

In addition, in the analysis of the coverage of the quadrivalent vaccine against HPV Alagoas, between 2014 and 2019, there was a drop in vaccine adherence over the years and that the highest coverages were referring to the year 2014 for girls and 2017 for boys.

It is worth noting that the limitations of this research were due to the use of secondary data that may not correspond to reality. In this perspective, the existence of underreporting of deaths by SIM was observed with considerable variation in coverage between Brazilian regions; high number of ignored fields, due to the lack of standardization in the collection and organization of data, making analysis difficult. Also, there were limitations regarding vaccination coverage, such as integration of the vaccine to the vaccination calendar only in 2014 and the change in the target age over the years, making it difficult to compare the data. Finally, the SI-PNI was still being implemented in part of the analyzed period.

Finally, the analysis made in this study can enable the creation of local strategies aimed at reducing CC mortality from the identification of factors and regions with vulnerability. In this sense, the importance of screening in mortality prevention is highlighted and, not least, the need to expand the publicity and significance of the HPV vaccination campaign, which showed a downward trend in the period studied.

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Received: 2024, July 18
Accepted: 2025, April 23