Cogitare Enfermagem

ORIGINAL ARTICLE

SPATIAL ANALYSIS AND TRENDS OF MORTALITY DUE TO PENILE CANCER IN SERGIPE, 2000 TO 2015

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ABSTRACT

Objective: To analyze the spatial distribution and temporal trend of mortality due to penile cancer in Sergipe.

Method: An ecological study with spatial analysis techniques. Secondary data on penile cancer deaths from residents of Sergipe municipalities from 2000 to 2015 were used, obtained from the Mortality Information System. The analysis of the temporal trends was performed in the Joinpoint program through Poisson regression. Spatial analyses were performed using the empirical Bayesian model, kernel estimator and Moran indexes.

Results: 67 deaths due to penile cancer occurred and a rising trend in mortality rates from 0.11 (2000) to 0.64 (2015) per 100,000 men was recorded. A positive spatial autocorrelation (I=0.64; p=0.01) was observed with areas of higher risk of death in the southern region of the state.

Conclusion: There was an increase in the coefficients of mortality due to penile cancer and heterogeneous geographical distribution of the risk areas.

DESCRIPTORS: Penile Neoplasms; Urological Neoplasms; Mortality; Time Series Studies; Spatial Analysis.

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ANÁLISE ESPACIAL E TENDÊNCIA DA MORTALIDADE POR CÂNCER DE PÊNIS EM SERGIPE, 2000 A 2015

RESUMO

Objetivo: analisar a distribuição espacial e a tendência temporal da mortalidade por câncer de pênis em Sergipe.

Método: estudo ecológico, com técnicas de análise espacial. Foram utilizados dados secundários dos óbitos por câncer de pênis de residentes dos municípios de Sergipe de 2000 a 2015, obtidos no Sistema de Informações sobre Mortalidade. A análise das tendências temporais foi realizada pelo programa Joinpoint por meio da regressão Poisson. As análises espaciais foram realizadas por meio do modelo bayesiano empírico, estimador de Kernel e Índices de Moran.

Resultados: ocorreram 67 óbitos por câncer de pênis e uma tendência crescente dos coeficientes de mortalidade, de 0,11 (2000) para 0,64 (2015) por 100.000 homens. Observou-se autocorrelação espacial positiva (I=0,64; p=0,01) com áreas de maior risco de morte localizadas na região sul do estado.

Conclusão: houve aumento dos coeficientes de mortalidade por câncer de pênis e distribuição geográfica heterogênea das áreas de risco.

DESCRITORES: Neoplasias Penianas; Neoplasias Urológicas; Mortalidade; Estudos de Séries Temporais; Análise Espacial.

ANÁLISIS ESPACIAL Y TENDENCIA DE LA MORTALIDAD POR CÁNCER DE PENE EN SERGIPE, 2000-2015

RESUMEN

Objetivo: analizar la distribución espacial y la tendencia temporal de la mortalidad por cáncer de pene en Sergipe.

Método: estudio ecológico, con técnicas de análisis espacial. Se utilizaron datos secundarios de las muertes por cáncer de pene en residentes de los municipios de Sergipe de 2000 a 2015, obtenidos del Sistema de Informaciones sobre Mortalidad. El análisis de las tendencias temporales se realizó en el programa Joinpoint por medio de la regresión Poisson. Los análisis espaciales se realizaron por medio del modelo bayesiano empírico, del estimador de Kernel y de los Índices de Moran.

Resultados: se registraron 67 muertes por cáncer de pene y una tendencia creciente de los coeficientes de mortalidad, de 0,11 (2000) a 0,64 (2015) por cada 100.000 hombres. Se observó una autocorrelación positiva (I=0,64; p=0,01) con áreas de mayor riesgo de muerte localizadas en la región sur del estado.

Conclusión: se registró un aumento de los coeficientes de mortalidad por cáncer de pene y una distribución héterogenea de las áreas de riesgo.

DESCRIPTORES: Neoplasias Penianas; Neoplasias Urológicas; Mortalidad; Estudios de Séries Temporales; Análisis Espacial.

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INTRODUCTION

Penile cancer is a type of genital tumor that, in a global context, has a low occurrence. It is estimated that approximately 26,000 cases are diagnosed annually worldwide[1]. It is a rare cancer in developed countries, but it has a high incidence in developing regions[2]. In the United States, for example, it causes about 300 deaths each year and accounts for approximately 1% of all male cancers[3]. Most cases of this malignancy occur in some regions of Africa, Asia and South America, where it represents about 10% of all the malignancies affecting men[1].

According to data from the José Alencar Gomes da Silva National Cancer Institute (*Instituto Nacional de Câncer*, INCA), in Brazil penile tumors represent 2% of all the cancers that affect the male population[4]. This reality is observed mainly in the North and Northeast regions, making these areas responsible for the largest number of new cases[4-5]. This fact can be explained due to the cultural and socioeconomic conditions of these regions[5].

Penile cancer also has a high mortality, which is due to the delay in seeking treatment. Commonly, the individuals who seek the health services present the disease at an advanced stage and progress, on average, from two to three years to death[6]. This high mortality can also be explained by the precarious socioeconomic conditions and the difficulty of access to the health services[5].

In this perspective, it is necessary to search for strategies that integrate the various conditions that make up the complex causality of penile cancer, valuing the socio-environmental aspects of the health-disease process. Given the problem, spatial analysis techniques stand out as important tools in understanding the geographical distribution of the disease, allowing to investigate possible correlations between the main causal factors, providing subsidies for risk stratification and better equationing of the prevention, diagnosis and disease control measures.

The aim of this study was to analyze the spatial distribution and temporal trend of penile cancer deaths in the state of Sergipe from 2000 to 2015.

METHOD

This is an ecological study of the time series type and with spatial analysis techniques performed in Sergipe, from 2000 to 2015. The state of Sergipe is located on the northeast coast of Brazil (Figure 1), is made up of 75 municipalities and its capital city is Aracaju. It has a population of approximately 2,278,308 inhabitants, an area of 21,910,354 km² and a demographic density of 94.3 inhabitants/km²[7].

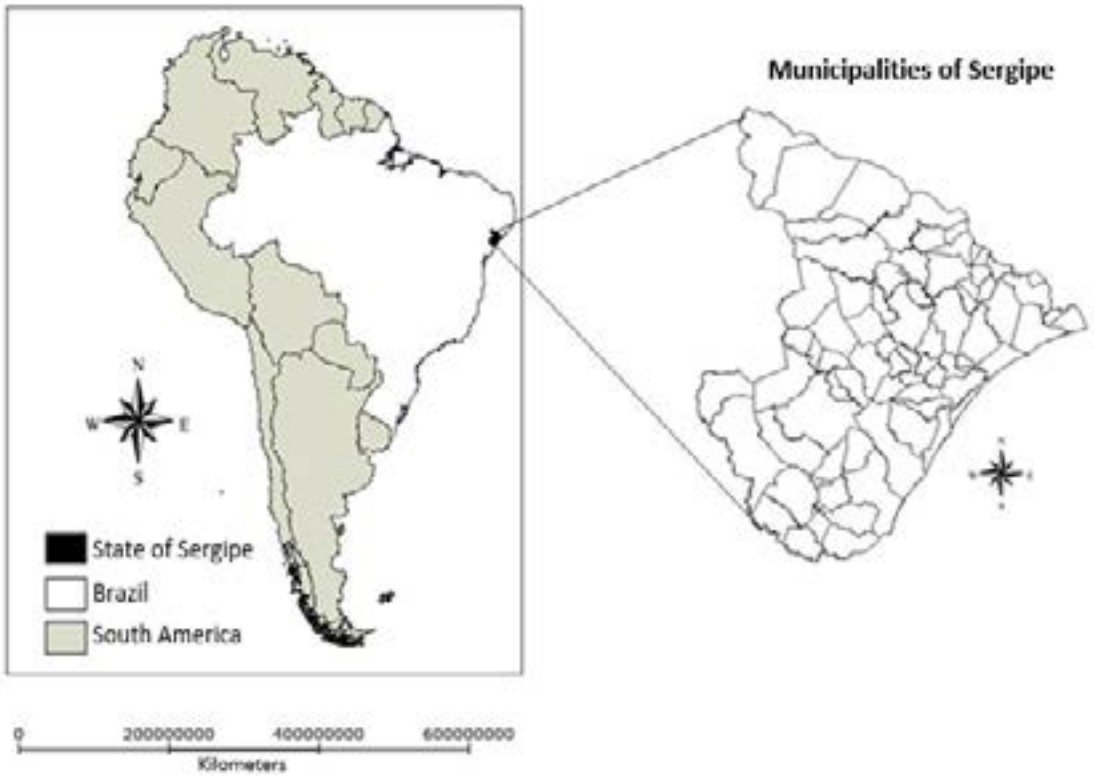

Figure 1 - Geographic localization of the state of Sergipe. Aracaju, SE, Brazil, 2019
Source: IBGE, 2010[7]

The codes C60 – C60.9, inserted according to the International Classification of Diseases (ICD)[8], which occurred in the municipalities of the state of Sergipe from 2000 to 2015, were considered penile cancer cases.

The study analysis comprised the following sociodemographic variables: age, race/skin color, marital status, education, place of occurrence and region of residence of the deaths.

Secondary data reported in the Mortality Information System (*Sistema de Informação sobre Mortalidade*, SIM) of the database of the Informatics Department of the Unified Health System (Datasus) were used[9].

The specific mortality coefficient for penile cancer was calculated from the following formula: [(Total deaths from penile cancer)/(Resident male population) x100,000].

The mortality coefficients were adjusted with the direct standardization method using the male standard population for the period studied. Data from the 2010 Population Census and the inter-census projections produced by the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística*, IBGE) were used[7] and made available by the Datasus[9].

Aiming to minimize possible biases, the national SIM database was compared with the state SIM data provided by the Sergipe State Health Department.

In the statistical analysis, the Bayesian Estimator was used to minimize the instability caused by the random fluctuation of the cases, smoothing the standardized coefficients by applying weighted means and creating a second corrected coefficient. The Empirical Bayesian Rate illustrated a multiplication rate correction of 100,000, taking into account the male population at risk and the number of cases for each year analyzed, by municipal area[10].

The time trends for the consecutive series were calculated using the penile cancer specific mortality coefficients as dependent variables and the year as the independent variable. The Joinpoint Regression Program Version 4.5.0.1 was used, by means of the Poisson regression method[11], to calculate the time trends of the frequency of absences with a model based on the assumption of a minimum number of points (Joinpoint) at which statistically significant changes in the time trends would occur. For this, a logarithmic linear model was performed, adding Joinpoints and calculating the difference up to a statistically significant value using the Monte Carlo permutation test[12]. In addition to time trends in the frequency of absences, the Annual Percentage Increments (Annual Percent Change - APC), were calculated.

In the spatial analysis, the location addresses of the deaths were geo-referenced and the points were marked by capturing the latitude and longitude coordinates provided by Google Maps[13]. Thematic maps of penile cancer mortality coefficients were constructed in the municipalities for the analyzed period. The Kernel intensity estimator was adopted which, through statistical smoothing, generated a density surface for the visual detection of "hot spots" indicating agglomeration on a spatial distribution and continuous surface from the data[10].

Spatial autocorrelation between the mortality coefficients was used to investigate whether the spatial distribution of the disease occurs randomly or follows any pattern of occurrence in the space. A spatial proximity matrix obtained by the contiguity criterion was elaborated, adopting a significance level of 5% and calculating the Global Moran Index (I) [14], varying from -1 to +1, which represents the expression of the spatial autocorrelation of mortality due to penile cancer in the geographic space analyzed to identify spatial clusters and risk areas. Values close to zero indicate spatial randomness; values between 0 and +1 indicate a positive spatial autocorrelation and values between -1 and 0, a negative spatial autocorrelation.

The Moran Scatter Diagram was used to indicate critical or transitional areas to compare the value of each municipality with the neighboring municipalities and to verify the spatial dependence shown by the Local Moran Index (Local Index of Spatial Association – LISA) for detection of regions with a significant spatial correlation[14].

Moran Maps were constructed for the spatial representation, considering municipalities with statistically significant differences ($p<0.05$)[14]. Thus, the distribution can be evidenced of the spatial patterns of possible clusters of risk for occurrence when the areas are formed by homogeneous areas of municipalities with high values of the rate, having as neighboring other municipalities with the same characteristic. Critical areas are those formed by areas within the Q1 (high/high) class of the Moran Map.

The cartographic base of the state of Sergipe was provided by the IBGE. The cartographic projection corresponded to the Universal Transverse Mercator (UTM) system, using the Terra Datum SIRGAS 2000 model (Geocentric Reference System for the Americas 2000). The descriptive data were tabulated and analyzed in GraphPad Prism version 5.01 and Microsoft Office Excel 2010. The TerraView 4.2.2 software[15] was used for the spatial analysis.

The study was approved by the Ethics and Human Research Committee of the University Hospital of the Federal University of Sergipe, under protocol No. 1,408,888.

RESULTS

From 2000 to 2015, 67 deaths due to penile cancer were recorded in the state of Sergipe. When analyzing the trend of the standardized penile cancer specific mortality coefficients, the number of junction points was zero and the whole series was considered as a single trend, with a significant increase over the period under study, with an APC of

11.91% (95% CI: 7.1 to 16.9; p=0.010). There has been a progressive increase in recent years, ranging from 0.11 deaths in 2000 to 0.64 deaths per 100,000 men in 2015. The mean coefficient of the deaths due to penile cancer in the period was 0.42 deaths per 100,000 men (Figure 2).

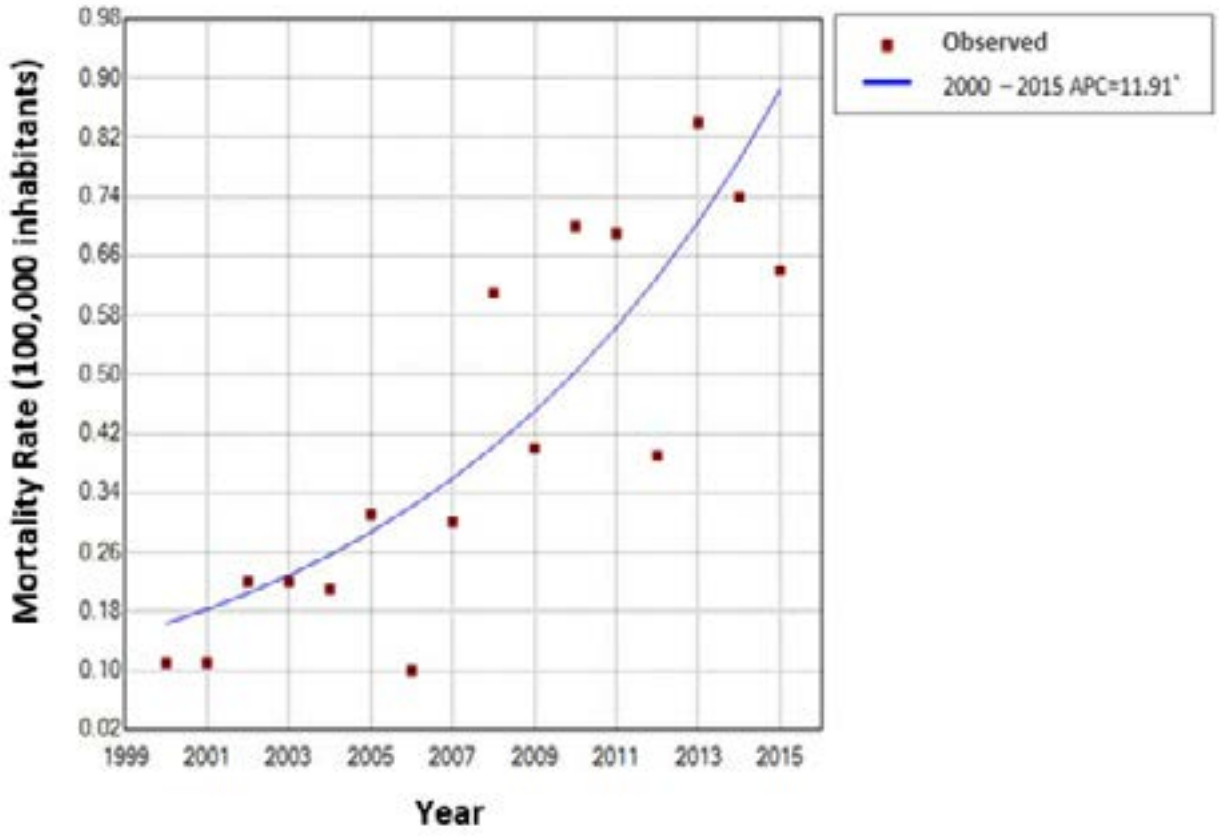

Figure 2 – Temporal trend of the standardized penile cancer mortality coefficients in the state of Sergipe between 2000 and 2015. Aracaju, SE, Brazil, 2019
Source: SIM/Datasus, 2018[9]

Table 1 shows that the highest percentage of deaths occurred in the age group of 60 years old or older, 40 (59.7%), brown race/skin color, 37 (55.2%), in married individuals, 35 (52.2 %), illiterate, 22 (32.2%), or one to three years of schooling, 16 (23.9%). It was found that most of the deaths occurred in hospital settings, 42 (62.7%), and among residents outside the metropolitan region, 45 (67.2%).

Table 1 - Sociodemographic characteristics of deaths due to penile cancer in the state of Sergipe between 2000 and 2015. Aracaju, SE, Brazil, 2019 (continues)

Sociodemographic variables	N (%)
Age group	
20 – 39	4(6)

40 – 59	23(34.3)
≥ 60	40(59.7)
Race/Skin color	
White	18(26.9)
Brown	37(55.2)
Black	4(6)
Asian	0(0)
Unknown	8(11.9)
Marital status	
Single	14(20.9)
Married	35(52.2)
Widow/Widower	5(7.5)
Others	13(19.4)
Schooling	
None	22(32.8)
1 to 3 years	16(23.9)
4 to 7 years	10(14.9)
8 to 11 years	6(9)
Unknown	13(19.4)
Place of occurrence	
Hospital	42(62.7)
Other health facilities	2(3)
Residence	23(34.3)
Region of residence	
Metropolitan area	21(31.3)
Other municipalities of the state	45(67.2)
Unknown	1(1.5)

Source: SIM/Datasus, 2018[9]

The spatial analysis techniques employed (Figure 3) showed a process of space conglomerates with a high variation in mortality due to penile cancer in the state of Sergipe. The Kernel estimator (Figure 3A) showed thickenings (hot spots) of the highest mortality coefficients located in three main regions: north, central east and south of the state. Areas of low occurrence of deaths due to penile cancer are observed in the northwest region.

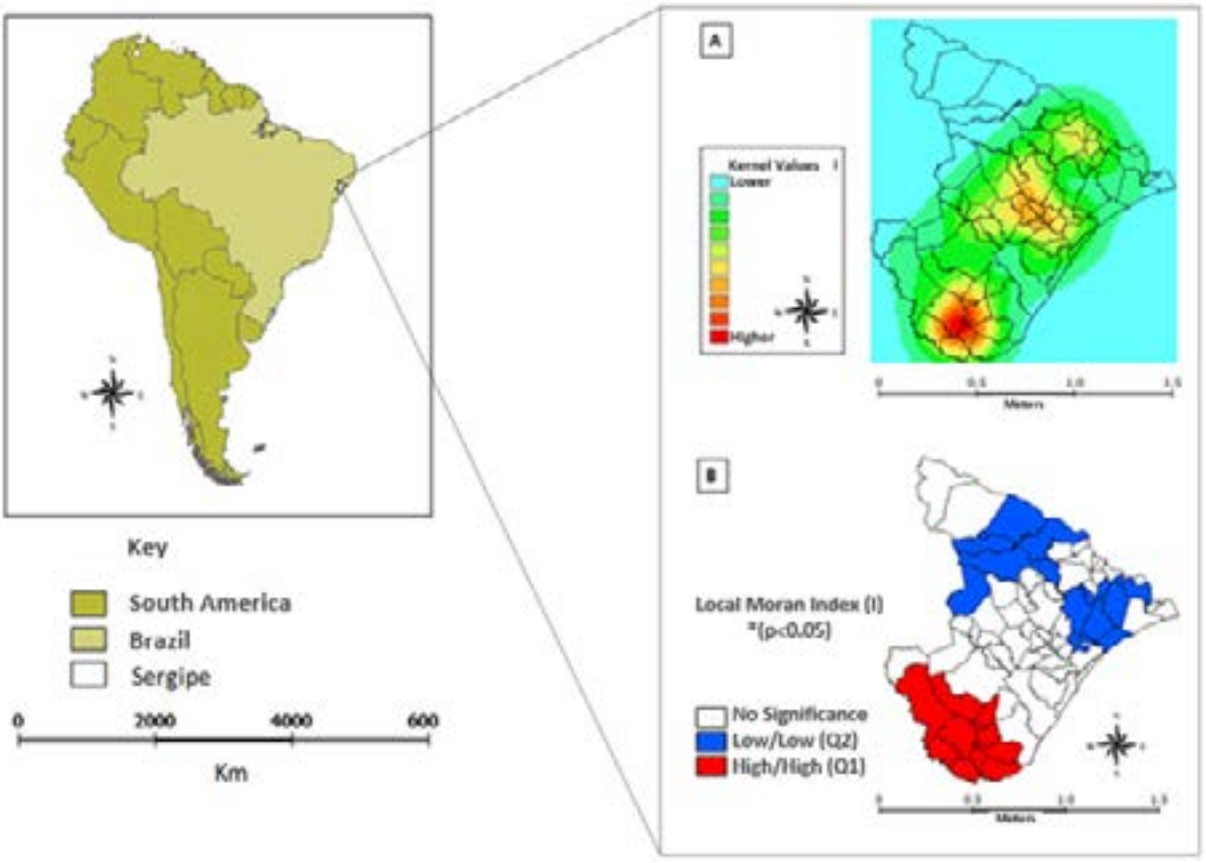

Figure 3 – Spatial analysis of the penile cancer mortality coefficients (A - Kernel Map; B - Moran Map) in the state of Sergipe between 2000 and 2015. Aracaju, SE, Brazil, 2019
Source: SIM/Datasus, 2018[9]

The spatial autocorrelation calculated by the Global Moran Index (I=0.64; p=0.010) was positive and significant for all the years studied (Table 2). The Moran's positive value indicated that municipalities with high incidence are likely to be close to other municipalities with high incidence and, conversely, municipalities characterized by low incidence are likely to be close to other municipalities with low incidence.

Table 2 – Global Moran Index of the penile cancer mortality coefficients in the state of Sergipe between 2000 and 2015. Aracaju, SE, Brazil, 2019 (continues)

Year	Value of the Global Moran Index (I)	p-value
2000	0.24	0.010
2001	0.15	0.010
2002	0.19	0.010
2003	0.24	0.010
2004	0.29	0.010
2005	0.39	0.010
2006	0.36	0.010
2007	0.38	0.010

2008	0.22	0.010
2009	0.07	0.010
2010	0.05	0.030
2011	0.31	0.010
2012	0.07	0.020
2013	0.24	0.010
2014	0.45	0.010
2015	0.14	0.010
Total period	0.64	0.010

Mortality due to penile cancer has increased in all regions, both inland and in the metropolitan region, but the southern and southwestern regions of the state have shown a significant and different pattern.

The Moran's maps (Figure 3B) show clusters of positive and significant autocorrelation. One cluster considered high risk for mortality due to penile cancer (high/high) was located in a continuous strip that extends from the south to the southwest of the state, comprising the municipalities of Arauá, Boquim, Cristinápolis, Indiaroba, Itabaininha, Pedrinhas, Santa Luzia Itanhy, Tomar do Geru, and Umbaúba. In addition to clusters of municipalities with low penile cancer mortality coefficients and neighbors with equivalent (low/low) values, located in the northeast regions (Capela, Carmópolis, Japaratuba, Japoatã, Muribeca, Neopolis, Pirambu, Rosario do Catete, and São Francisco) and northwest of the state (Carira, Gararu, Gracho Cardoso, Monte Alegre de Sergipe, Nossa Senhora da Gloria, and Porto da Folha). The municipalities of the metropolitan region of Sergipe belong to a low risk cluster despite the non-statistical significance.

DISCUSSION

The present study shows that the penile cancer mortality coefficient in Sergipe showed a significant increase in the studied interval, with a mean death coefficient of 0.42 per 100 thousand men. This reality is similar to a study conducted in Pernambuco, which found that, from 2000 to 2009, there was an increase in the mortality coefficient for penile carcinoma, from 0.34 to 0.42 per 100 thousand men, and a mean of 0 45 deaths per 100,000 men[16].

High mortality may be related to the delay in seeking treatment[6], since the penis, the male organ with attributes related to virility and masculinity, can represent the essence of being male. Penectomy, one of the proposed treatments, is a mutilating surgery, capable of causing feelings of anguish in the face of lack of self-esteem, as well as repercussions on sexual, affective and social life[17].

According to data from the Demographic Census conducted in 2010 by the IBGE, of the 27 federative units, Sergipe occupies the 19th position in the ranking of the Human Development Index (HDI) in Brazil[7]. This information reflects the importance of the relationship between the low socioeconomic status and the development of penile neoplasms[18], which may have contributed to the increase in the mortality coefficients for this cancer in the state.

It is also inferred that the increase in the number of deaths may occur due to the

period of epidemiological and demographic transition that Brazil and, consequently, the state of Sergipe is going through in recent years. There is an important change in the profile of morbidity and mortality, making chronic degenerative diseases, including various cancers, penile cancer included, stand among the leading causes of death in the Brazilian male population[19].

Regarding the risk of death due to penile neoplasia, a study conducted in 2013 predicted an increase in the number of cases for the 2011-2025 period, due to the high rate of infection by the Human Papilloma Virus (HPV), consequently leading to an increase in the number of deaths[20].

Infection with certain HPV subtypes has been correlated as a major risk factor for the development of penile cancer. The overall prevalence of HPV infection related to penile carcinoma is estimated to be 42% to 48%, with subtypes 16 and 18 being the most commonly involved[18].

A higher mortality due to the disease was observed from the sixth decade of life. These findings are similar to those found in national studies conducted from 2006 to 2007[5] and in 2013[21], and international studies carried out in Chile from 1996 to 2006(6), and in Sweden from 2000 to 2012[22]. In this age group, the coincidence between the onset of malignancy and the evolution of death is due to the aggressiveness and rapid evolution of the tumor[6].

Regarding race/skin color, there was hegemony of deaths in brown men, although there is limited scientific literature regarding racial or ethnic preponderance in penile cancer[5]. In an analysis performed in Pernambuco, between 2000 and 2009, there was also a predominance of deaths due to penile cancer in brown men[16]. Data from the National Household Sample Survey (*Pesquisa Nacional Por Amostra de Domicílios*, PNAD), conducted by the IBGE in 2015, show the predominance of brown individuals in the male population in Sergipe[23], probably justifying the greater involvement of this ethnicity in the state.

Most of the occurred in married men, consistent with the reality observed from 2007 to 2012, in two referral centers in the state of Pernambuco[21], and in a retrospective study conducted in the state of Maranhão with men diagnosed with penile cancer during the period 2004-2014[24]. It is understood that there is a possible influence exerted by the spouse to seek treatment, impacting on the diagnosis of the disease and thus on the number of new cases and deaths[25].

In addition to HPV, persistence of phimosis, poor conditions of intimate hygiene and low education are factors closely related to the development of penile carcinoma[4]. These are data that corroborate the present study, in which illiteracy and low schooling were predominant variables in the studied population.

The study points out that 62.7% of the deaths occurred in a hospital environment. This reality is consistent with a study conducted in Londrina-PR, from 1996 to 2010, which showed a significant increase in the rate of deaths in hospitals, especially when referring to the population over 60 years old[26]. This behavior is directly related to the increased demand for health services that support the death process, as well as the changes in the health policies[26].

There was a predominance of deaths in men who lived outside the metropolitan region of the state, in disagreement with studies conducted in the state of Pernambuco, which observed greater involvement of men living in the metropolitan region[16,21]. The centralization of high complexity oncology services in the metropolitan region of Aracaju, capital of Sergipe[27], may have contributed to the increased death toll in other regions of the state. Difficulty in accessing more complex care levels may make timely diagnosis and treatment impossible[5], eventually contributing to a greater number of deaths in distant municipalities of the capital.

Health geo-processing is a technology used to assess the health status of populations and to identify regions and groups at risk, performing analysis of the spatial spread of diseases and their relationships with different environments[28].

The spatial analysis techniques employed allowed for the identification of areas that deserve to be highlighted in relation to the risk of death due to penile cancer. The Kernel estimator produced a continuous surface, with densities calculated at all locations based on the total number of cases and without considering the geographic boundaries of the municipalities[10].

The Kernel technique has greater advantages for the quick visualization of areas that deserve attention, besides being unaffected by the political-administrative division[10], while the Moran's technique constructed maps considering the state's political-administrative divisions and the clusters are based on the number of cases by the population rates of the municipalities[14]. Thus, an area with high risk for mortality was observed, extending from the south to the southwest of the state of Sergipe, while some municipalities in the northwest and northeast of the state were characterized as low risk.

One factor that may possibly explain the large number of concentrated cases in the municipalities of southern and southwest Sergipe, would be the fact that the state of Sergipe is one of the main agricultural producers in the Northeast, highlighting most of these municipalities as major citrus producers of the state, and where a large contingent of people involved in agriculture and less educated are concentrated[29].

A prolonged exposure of the general population to the various types of pesticides used in this region is also suggested as a cause. In an epidemiological study conducted with farmers of a banana plantation in Costa Rica from 1981 to 1992 it was shown that the risk for the occurrence of any cancer increased with the exposure time to pesticides, penis carcinoma being one of the most frequent among the men studied[30]. However, it is important that further investigation be conducted on the contact with pesticides and on the development of this malignancy[30].

Further investigations should be performed to better understand the high mortality due to penile cancer in the south and southwest of the state of Sergipe. The limitations of the study relate to the use of secondary data and their inherent problems with underreporting of cases in the information system (SIM) used. In order to reduce possible inconsistencies, the national SIM database was compared with the state SIM data provided by the Sergipe State Health Department.

CONCLUSION

The present study contributes to the identification of the epidemiological profile of deaths due to penile cancer in Sergipe, supporting the elaboration and implementation of public policies aimed at the prevention of penile cancer through a spatial and behavioral risk approach. The spatial analysis techniques made the study feasible and became an important methodological tool for a better knowledge of this problem and to better define the main risk areas.

It was concluded that there was an increase in the penile cancer mortality rates in Sergipe and that the geographic distribution of the areas at risk of death due to penile carcinoma was heterogeneous, based both on the amplitude of the territory and on the concentration of cases in certain regions.

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