Cervical Cancer Mortality in Northeastern Municipalities: Correlation with Sociodemographic Indicators

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Mortalidade por Câncer do Colo do Útero nos Municípios Nordestinos: Correlação com Indicadores Sociodemográficos

Mortalidad por Cáncer de Cuello Uterino en Municipios del Nordeste: Correlación con Indicadores Sociodemográficos

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ABSTRACT

Introduction: Cervical cancer mortality is considered preventable. High rates and an upward temporal trend and observed in Brazil's Northeast. **Objective**: To evaluate the spatial distribution of cervical cancer mortality of municipalities in Brazil's Northeast in the period 2015-2019 and its correlation with sociodemographic indicators. **Method**: Mortality data were obtained from DATASUS Mortality Information System. Mortality rates per 100,000 women were calculated and smoothed using the empirical Bayesian estimator. The spatial correlation of mortality rates was evaluated using the global and local Moran index. Moreover, the correlation between mortality rates and sociodemographic indicators was tested using bivariate analysis. Mapping and analyzes were performed using GeoDa and R software, values of $p<0.05$ were considered statistically significant. **Results**: Rates ranged from 1.0 to 27.2 deaths per 100,000 women, with the highest rates concentrated in the municipalities of Maranhão, Piauí, Ceará, Alagoas, and Sergipe. Clusters with high mortality were observed in the municipalities of Maranhão and Piauí (close to Maranhão) on the coast of Pernambuco, Alagoas, Sergipe, and Bahia. An association between socioeconomic indicators and mortality by cervical cancer was found. Municipalities with the worst indicators show higher mortality rates by this neoplasm. **Conclusion**: High mortality rates were observed in municipalities with the worst sociodemographic indicators, indicating the health system's limitations in reducing these rates in cities with low socioeconomic development.

Key words: uterine cervical neoplasms/mortality; spatial analysis; health status indicators; socioeconomic factors.

RESUMO

Introdução: A mortalidade por câncer do colo do útero é considerada evitável. Altas taxas e tendência ascendente são observadas no Nordeste do Brasil. **Objetivo:** Avaliar a distribuição espacial da mortalidade por câncer do colo do útero nos municípios do Nordeste do Brasil no período 2015-2019 e sua correlação com indicadores sociodemográficos. **Método:** Os dados de mortalidade foram obtidos junto ao Sistema de Informação sobre Mortalidade do DATASUS. Calcularam-se as taxas de mortalidade por 100 mil mulheres, suavizadas por meio do estimador bayesiano empírico. Avaliou-se a correlação espacial das taxas de mortalidade por meio do índice de Moran global e local. E testou-se a correlação das taxas de mortalidade com os indicadores sociodemográficos por meio da análise bivariada. O mapeamento e as análises foram realizados nos *softwares GeoDa* e *R*, e considerados estatisticamente significativos valores de $p<0,05$. **Resultados**: As taxas variaram de 1,0 a 27,2 óbitos por 100 mil mulheres, com as maiores taxas concentradas nos municípios do Maranhão, Piauí, Ceará, Alagoas e Sergipe. *Clusters* com alta mortalidade foram observados nos municípios do Maranhão e do Piauí (próximo ao Maranhão), no litoral de Pernambuco, Alagoas, Sergipe e Bahia. Verificou-se associação entre os indicadores socioeconômicos e a mortalidade por câncer do colo do útero. Localidades com os piores indicadores mostram maiores taxas de mortalidade por essa neoplasia. **Conclusão**: Observaram-se altas taxas de mortalidade nos municípios com piores indicadores sociodemográficos, indicando as limitações do sistema de saúde para reduzir essas taxas nas cidades com menor desenvolvimento socioeconômico.

Palavras-chave: neoplasias do colo do útero/mortalidade; análise espacial; indicadores básicos de saúde; fatores socioeconômicos.

RESUMEN

Introducción: La mortalidad por cáncer de útero se considera prevenible. Se observan tasas elevadas y una tendencia al alza en el Nordeste de Brasil. **Objetivo**: Evaluar la distribución espacial de la mortalidad por cáncer de cuello uterino en municipios del Nordeste de Brasil en el período 2015-2019 y su correlación con indicadores sociodemográficos. **Método**: Los datos de mortalidad se obtuvieron del Sistema de Información de Mortalidad DATASUS. Se calcularon las tasas de mortalidad por 100 000 mujeres, suavizadas mediante el estimador empírico bayesiano. La correlación espacial de las tasas de mortalidad se evaluó mediante el índice de Moran global y local. Y se probó la correlación entre las tasas de mortalidad y los indicadores sociodemográficos mediante análisis bivariado. El mapeo y los análisis se realizaron utilizando los *softwares GeoDa* y R, y valores de $p<0,05$ se consideraron estadísticamente significativos. **Resultados**: Las tasas oscilaron entre 1,0 y 27,2 muertes por 100 000 mujeres, con las mayores tasas concentradas en los municipios de Maranhão, Piauí, Ceará, Alagoas y Sergipe. Se observaron conglomerados con alta mortalidad en los municipios de Maranhão y Piauí (cerca de Maranhão), en el litoral de Pernambuco, Alagoas, Sergipe y Bahia. Hubo una asociación entre los indicadores socioeconómicos y la mortalidad por cáncer de cuello uterino. Las localidades con peores indicadores presentan mayores tasas de mortalidad por esta neoplasia **Conclusión**: Se observaron altas tasas de mortalidad en los municipios con peores indicadores sociodemográficos, lo que indica las limitaciones del sistema de salud para reducir estas tasas en los municipios con menor desarrollo socioeconómico.

Palabras clave: neoplasias del cuello uterino/mortalidad; análisis espacial; indicadores de salud; factores socioeconómicos.

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INTRODUCTION

Cervical cancer (CC) maintains high incidence and mortality rates in low- and middle-income countries. Unjustifiable reality, as such neoplasm has primary prevention, the vaccine against human papillomavirus (HPV), and secondary, the Pap smear, which, in addition to preventing, also enable the control of the disease[1].

Diagnostic and treatment medical technologies for CC are not equally distributed among countries in the world. Worse conditions of access to preventive and curative medical services and technologies are more prevalent in middle-and low-income countries, contributing to more than 80.0% of new cases and deaths occurring in countries with high socio-economic vulnerability[1-4].

Likewise, in Brazil, in the Federative Units (UF) with greater socioeconomic vulnerability and health inequalities, CC is the second most frequent cancer, excluding non-melanoma skin cancers, surpassed only by breast cancer[5]. In the South and Southeast Regions, this disease is the third most frequent, surpassed by new cases of breast, colon and rectal cancer[5]. Thus, it is noteworthy that the incidence rate per 100,000 women estimated for the North Region is 1.6 higher than the rates in the Southeast Region (20.48 *vs.* 12.93) and the expected incidence rate for the Northeast is 1.4 higher than that of the Southeast (17.59 *vs.* 12,93)[5]. Inequalities that are also observed in the magnitude and evolution over time of mortality rates from this neoplasm[6-11].

Also, it is important to note that in the FUs of the North and Northeast, higher mortality rates due to CCU and greater magnitude of the percentage of records whose underlying cause of death was classified as unspecified portion of uterine cancer (NEP) were observed, compared to the states of the South and Southeast[7,8]. Reinforcing health inequalities, while in the Southern and Southeastern States there was an increase in mortality rates due to CC and a reduction in the relative risk of death in the five-year period from 2005 to 2019 compared to the period from 1995 to 1999, in the Northern and Northeastern States there was an increase in this health indicator and an increase in the risk of death due to CC[7,8]. Persistent health inequities, despite the fact that Brazil has a National Cancer Control Program (PNCC) of universal and free access, with guidelines on the target population, frequency of examinations, referral for the treatment of precursor lesions and the CCU[6-11].

The disparities observed in the incidence and mortality due to CC are related to the temporal and spatial distribution of the magnitude of the proportion of risk and protective factors in the female population[1-4]. Among the main risk factors, we highlight the use of oral contraceptives, the fertility rate, behaviors that increase the risk of HPV infection, in addition to the incidence of diseases that reduce women 'simmunity[1-4]. Regarding the main protective factors, we highlight the high coverage of the HPV vaccine, the presence of an organized screening program with high coverage and quality correlated with access to treatment of the disease and its precursor lesions in a timely manner (surgery, chemotherapy and radiotherapy).

In Brazil, it is known that risk and protection factors are not evenly distributed among the FUs and within their municipalities[6-11]. Therefore, there is a higher fertilityrate[12], lower coverage of gynecological preventive, greater deficit in the performance of Pap smears[13,14] and in the quantity of biopsies in the States of the Regions of greater socioeconomic vulnerability (North and Northeast)[15]. In these locations, there is also a lower concentration of chemotherapy and radiotherapy services[16], factors that contribute to the persistence of high mortality rates due to CC, with Maranhão and Piauí[7,9] presenting mortality rates similar to those of countries that do not have a universal and free access screening program[1].

Based on the above, this study aimed to analyze the spatial occurrence of CC mortality in municipalities in the Northeast of Brazil in the period 2015-2019 and its correlation with sociodemographic indicators. In order to identify the municipalities and regions with the highest mortality rates and thus provide subsidies for the prevention and control of this disease. Primary Health Care (PHC) has its activities at the municipal level, being responsible for the activities of attracting women, collecting, and referring them for the treatment of precursor lesions and CCU[16-20].

METHOD

An observational study of ecological design with spatial cutout at the municipal level, which followed the recommendations of the *Guidelines for Accurate and Transparent Health Estimates Reporting: the GATHER statement*[21].

The response variable of this study was the mortality rate from CC per 100,000 women, aged 20 years or older, for each municipality in the five-year period from 2015 to 2019. It was decided to study mortality in this five-year period, since in a previous study, there was an increase in the risk of death in most of the Northeastern States, in the periods 2005-2009 and 2010-2014[7].

Death data were obtained from the Mortality Information System of the Department of Informatics of the Unified Health System (SIM/DATASUS)[22], extracting the records with the following characteristics: female sex;

age from 20 years; year from 2015 to 2019; municipalities in the Northeast; and the codifications C53 (cervical cancer); C54 (cancer of the body of the uterus); and C55 (cancer of the uterus of unspecified portion) of the Tenth International Statistical Classification of Diseases and Related Health Problems (ICD-10)[23]. The population estimates used in the present study were those estimated by Freire et.al.[24] for small areas.

The SIM/DATASUS[22] microdata of the municipalities for the years 2015 to 2019 were retrieved for each State in the *Northeast Region,* through the Tabwin version 4.15 for *Windows* program made available by the Ministry of Health (MS) of Brazil, *later grouped* in a single database for all municipalities through the *R* software (version 4.2.0).

In this first stage, there was a high percentage of deaths classified as PNE, that is, cancers of the uterus in which it is not possible to determine the location of the disease, cervix or body of the uterus, because of the late diagnosis of the disease[6-10], knowing that, as pointed out by other studies, many cancers thus classified are actually CCU[6-10]. The present study, with the purpose of improving the quality of death records, performed the correction of death records using the methodology proposed by Loos et al.[25], that is, proportionally redistributing deaths classified as PNE according to year, age group and location, to the records of CC and cancer of the uterine body according to the percentage of records originally certified for each of these causes of death. The rectification process was carried out by two researchers independently, confirmed by a third party, in order to ensure greater reliability of this process. All correction steps were performed in the *R software* (version 4.0.2).

Corrected deaths, mortality rates were calculated according to age groups, standardized by the direct method, with the standard population proposed by Segi modified by Doll et al.[26]. This standardization aimed to control the effect of the different age structures of the municipalities under study on the magnitude of mortality rates. After this process, smoothed mortality rates were estimated using the global empirical Bayesian estimator. This estimator calculates a global average for each city, comparing the population quantity with that of neighboring cities, which reduces the risks of instability of rare event expression in the population of municipalities with a lower population quantity[27-29]. Neighboring municipalities were considered to be those that share at least one side in common, according to the connectivity criterion[27-29].

After smoothing the rates, the mortality rates were mapped, using the digital meshes referring to the nine states of the Northeast Region, with the representation of the municipalities, made available in the database of the Brazilian Institute of Geography and Statistics (IBGE)[30], and the legends elaborated from the soft break. In addition, the hypothesis of dependence in the space of mortality rates due to CC was tested by the global Moran index. This index analyzes how the values observed in a spatial unit are correlated with the rates of its neighbors[27,28]. Next, the local Moran index was estimated to identify the presence of conglomerates of municipalities with similar behaviors in relation to their neighbors[26-28].

Then, the correlation between the response variable (CC mortality rates) and the independent variables – Municipal Development Index of the Federation of Industry of the State of Rio de Janeiro (FIRJAN) – was analyzed using the bivariate global Moran index[26-28]. All analyzes were *performed* using *GeoDa* software version 1.20.0.8, and p values < 0.05were considered statistically significant.

We chose to use the FIRJAN Municipal Development Index (IFDM)[31] of national scope, with base year 2016, as they were the most updated data considering the time frame of the present study (2015-2019). The IFDM is composed of three areas of assessment: Employment/ Income, Education and Health, with values ranging from zero to one, with an interpretation similar to the Human Development Index (HDI)[31].

The variables that make up the IFDM Education are attendance at early childhood education; dropout from elementary school; age-grade distortion in elementary school; teachers with higher education in elementary school; average daily class hours in elementary school; and result of the Basic Education Development Index (IDEB) in elementary school. It is noteworthy that the components of the IFDM Health mostly assess the quality of PHC: proportion of adequate prenatal care; deaths from ill-defined causes; infant deaths from preventable causes; and hospitalization sensitive to primary care (ISAB)[31].

The research was carried out with open access data from SIM/DATASUS in which there is no identification of the subjects and, therefore, there was no need to submit it to the Research Ethics Committee in accordance with art. 1 of CNS Resolution nº. 510, of April 7, 2016[32].

RESULTS

In the Northeast, between 2015 and 2019, there were 12,344 deaths from CC (9.8 deaths/100,000 women), 2,648 deaths from PNE (2.7 deaths/100,000 women) and 1,703 from uterine cancer (1.7 deaths/100,000 women). Higher rates of deaths classified as PNE per 100,000 women were verified in the states of Rio Grande do Norte (4.0 deaths/100,000 women) and Paraíba (3.1 deaths/100,000 women). After the rectification process,

there was a 27.3% increase in mortality rates in the Northeast Region (12.5 deaths/100,000 women), with the percentage increase ranging from 12.9% (Maranhão) to 40.0% (Rio Grande do Norte) (Table 1).

After the correction of deaths, higher mortality rates per 100,000 women were observed in the states of Maranhão (17.1 deaths/100,000 women) and Piauí (14.0 deaths/100,000 women) and the lowest in Bahia (10.2 deaths/100,000 women) and Rio Grande do Norte (11.0 deaths/100,000 women). The standardized and smoothed mortality rates according to the municipalities of the Northeast showed a minimum rate of 1.0 deaths per 100,000 women and a maximum of 27.2 deaths per 100,000 women. The highest rates are concentrated in the municipalities of Maranhão, Piauí (near Maranhão), on the coast of Pernambuco, Alagoas, Sergipe, and Bahia (Figure 1). It is noteworthy that 40% of the ten municipalities with the highest mortality rates per 100,000 women are located in the State of Maranhão: Morros (23.9 deaths/100,000 women); Chapadinha (23.3 deaths/100,000 women); Boa Vista do Gurupi (23.2 deaths/100,000 women); and Presidente Sarney (22.2 deaths/100,000 women). On the other hand, 60% of the ten municipalities with the lowest mortality rates are located in the State of Bahia: Maetinga (5.2 deaths/100,000 women); Igapora (5.1 deaths); Rio do Antonio (5.1 deaths/100,000 women); Jacaraci (4.51 deaths/100,000 women); Pindaí (4.4 deaths/100,000 women); and Valenca (4.3 deaths/100,000 women) (Figure 1).

After estimating the overall Moran index (Moran index =0.63; p <0.05), the hypothesis of spatial dependence

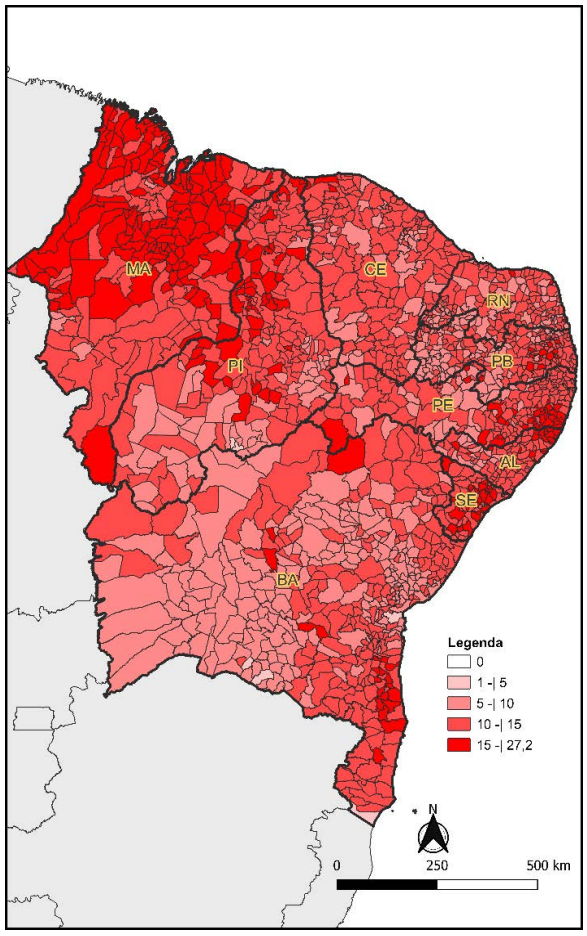

Figure 1. Corrected, standardized and smoothed mortality rates for CC in municipalities in Northeastern Brazil, 2015-2019

Source: SIM[22] and populations estimated by Freire et al.[24].
Captions: AL = Alagoas; BA = Bahia; CE = Ceara; MA = Maranhão; PB = Paraíba; PE = Pernambuco; PI = Piauí; RN = Rio Grande do Norte; SE = Sergipe.

Table 1. Mortality rates per 100,000 women for UCC, uterine cancer, PNE uterine cancer, corrected UCC, according to States of the Northeast Region, 2015-2019

Locations	CCU	PNE	Cancer of the body of the uterus	CCU corrected	Δ%
Alagoas	9.6	2.8	1.9	12.5	29.3
Bahia	7,6	2.4	1.4	10.2	34.6
Ceará	9.6	2.0	1.9	12.0	24.8
Maranhão	15.4	3.1	1.2	17.4	12.9
Paraíba	9.6	3.1	1.6	12.7	32.8
Pernambuco	9.9	2.3	2.9	13.0	31.3
Piauí	11.9	2.7	1.0	14.1	19.0
Rio Grande do Norte	8.3	4.0	1.4	11.0	32.0
Sergipe	10.0	2.6	1.5	14.0	40.0
Northeast Region	9.8	2.7	1.7	12.5	27.3

Source: SIM[22] and populations estimated by Freire et al.[24].
Captions: CCU = cervical cancer; PNE = uterine cancer of unspecified portion; corrected CCU = cervical cancer corrected according to the methodology proposed by Loos et al.[25]; Δ%= percentage variation of corrected CCU mortality rates compared to uncorrected CCU mortality rates. (a) mortality rates standardized by the direct method with the standard population proposed by Segi modified by Doll et.al.[26].

between mortality rates due to CC in municipalities in the Northeast was proven. Also, the local Moran index showed the existence of spatial *clusters* of high mortality rates in the municipalities of Maranhão, Piauí (neighboring Maranhão) and on the coast of Pernambuco, Alagoas, Sergipe and Bahia (Figure 2).

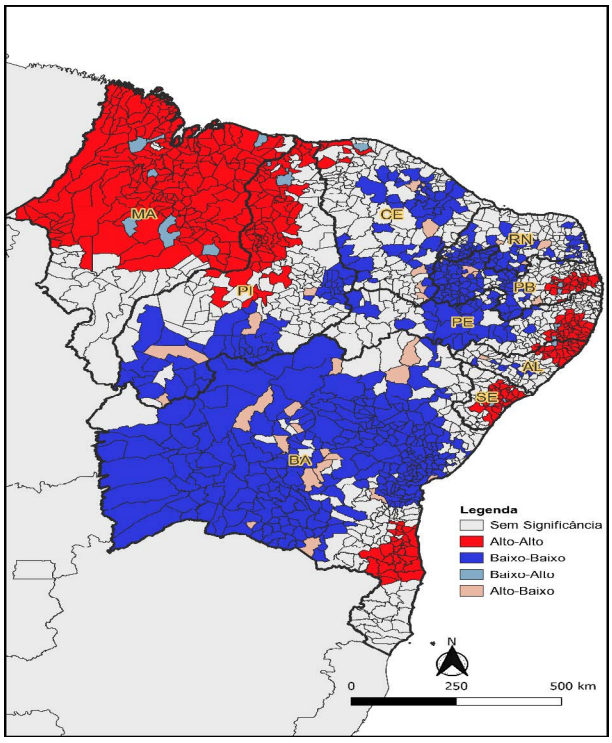

Figure 2. Moran's Local Map for the detection of spatial clusters of CC mortality rates for municipalities in Northeastern Brazil, 2015-2019

Source: SIM[22] and populations estimated by Freire et al.[24].
Captions: AL = Alagoas; BA = Bahia; CE = Ceara; MA = Maranhão; PB = Paraíba; PE = Pernambuco; PI = Piauí; RN = Rio Grande do Norte; SE = Sergipe.

High mortality rates due to CCU in the Northeast were presented in the municipalities that showed lower values of total IFDM, IFDM-Education and IFDM-Health, especially in the municipalities of Maranhão and Piauí near the State of Maranhão and the coast of Bahia (Figures 3 and 4).

DISCUSSION

The Brazilian Northeast presents high socioeconomic vulnerability and health inequalities, resulting from the Brazilian colonization process that generated regional inequalities that are maintained to the present day[33,34]. This cooperates with the higher proportion of residents in these areas of Brazil who refer to their own health as very bad or bad, with restricted activities and a lower percentage of medical consultations and use of health services in the last year, in addition to the lower coverage of gynecological

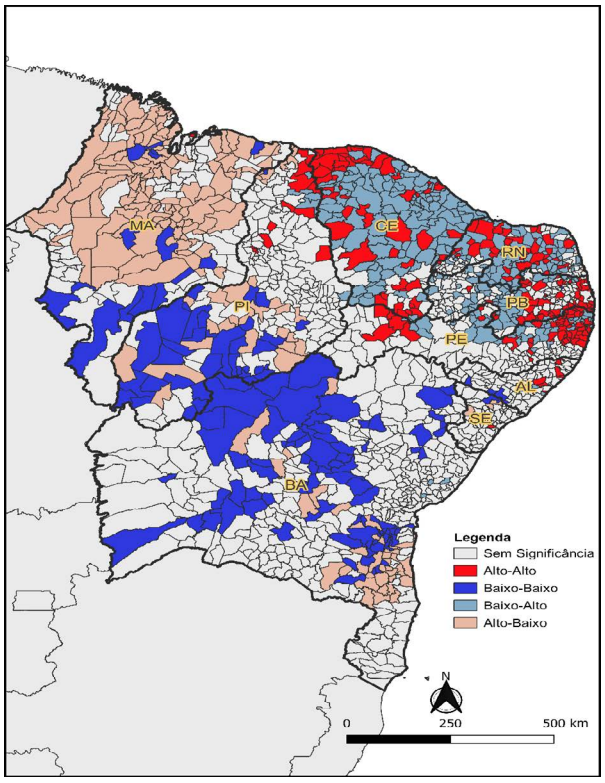

Figure 3. Moran's Local Map for the detection of the correlation between CC mortality rates and IFDM for municipalities in Northeastern Brazil, 2015-2019

Source: SIM[22] and populations estimated by Freire et al.[24].
Captions: AL = Alagoas; BA = Bahia; CE = Ceara; MA = Maranhão; PB = Paraíba; PE = Pernambuco; PI = Piauí; RN = Rio Grande do Norte; SE = Sergipe.

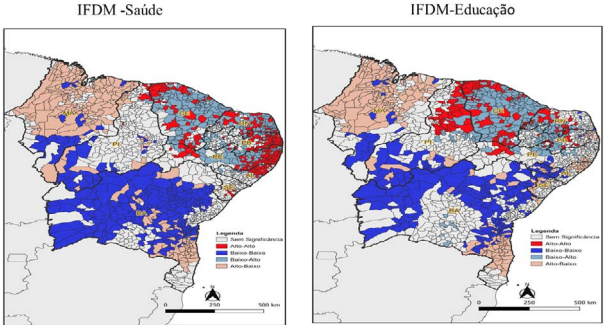

Figure 4. Moran's Local Map for the detection of the correlation between CC mortality rates and IFDM for municipalities in Northeastern Brazil, 2015-2019

Source: SIM[22] and populations estimated by Freire et al.[24].
Captions: AL = Alagoas; BA = Bahia; CE = Ceara; MA = Maranhão; PB = Paraíba; PE = Pernambuco; PI = Piauí; RN = Rio Grande do Norte; SE = Sergipe.

prevention and mammography, when compared to the South and Southeast[35,36].

Inequalities contribute to the result observed in the present study of a high proportion of records classified as PNE, with mortality rates due to this coding higher than those due to cancer of the uterine body, including in municipalities with greater socioeconomic development. Findings that indicate the low efficacy and effectiveness

of the PNCC, since a large portion of the population of these locations did not have access to timely diagnosis and treatment of their disease[13-15].

This situation is disturbing, since, in the 2000s, Brazil experienced the expansion of access to health and increased coverage of the Family Health Strategy (FHS) and improvements in access to Oncological Care were observed due to the expansion of the Oncological Care Network[16-18]. In this sense, a significant reduction in new cases, CC mortality and death records classified as PNE[18] was expected.

However, as in a previous study, there was a higher percentage of deaths from PNE (C55) in municipalities in the countryside compared to the capitals (1996 to 2005)[9]. In the same direction, a higher proportion of deaths due to this coding was evidenced in the health regions of Rio Grande do Norte located in the semi-arid region (1996-2010)[37]. Thus, these studies showed a greater magnitude and upward trend in CC mortality rates in municipalities in the interior of the Northeast[9] and in the semi-arid health regions of Rio Grande do Norte[37]. Reality that was maintained in the present study, higher mortality was verified in the countryside municipalities of Maranhão and Piauí, in addition, only 0.4% of the northeastern municipalities presented mortality rates per 100,000 women lower than the value recommended by the World Health Organization (WHO) (5.0 deaths/100,000 women)[1].

In the first years after the implementation of a universal access CC screening program, an increase in mortality is expected, as many women who did not have access to this diagnostic method can be diagnosed at an advanced stage[1,4]. However, when the program achieves high coverage of the target population, with high-quality examinations, the timely diagnosis of high- and low-grade premalignant lesions is expanded, promoting the reduction of new cases and mortality[1,4]. However, in Brazil, more than two decades after the beginning of the PNCC, high incidence and mortality rates are still observed in the states and municipalities of the North and Northeast[5,7,8].

Mortality from CC, a disease associated with infection, has a strong correlation with the worst socioeconomic indicators, confirming the cancer transition presented by Bray et.al.[38]. Cancers associated with infection are more prevalent and incident in territories with high socioeconomic vulnerability, while those associated with westernization of habits and lifestyle have higher rates of incidence, prevalence, and mortality in high-income countries[1,39]. In this sense, a Brazilian study showed higher mortality rates from CC and lower rates of breast cancer in Brazilian municipalities with lower HDI. An inverse profile was found in cities with higher HDI[38,39].

The findings of other studies showed a correlation between mortality from CC and socioeconomic conditions[1,9,38,39]. In this study, there was a positive correlation between the high mortality rates from this neoplasm and the cities with the worst socioeconomic and health conditions according to the total IFDM, IFDM-Health and IFDM-Education. In the same direction, the study by Gamarra et al.[9] demonstrated a positive correlation between CC mortality and the following indicators: proportion of illiterate people aged 25 years or more; percentage of inhabitants below the poverty line; and mortality rate up to five years[9].

In addition, in the present study, there was a higher percentage of cities with high mortality rates in states with lower socioeconomic development (Maranhão and Piauí), with rates similar to those of countries that do not have a universal access screening program[1]. Findings that may be correlated with the operationalization of the Brazilian screening program, which is not organized, but opportunistic, contributing to the maintenance of low coverage in black and indigenous women, with low education and living in territories with greater socioeconomic inequality and health inequalities[13,14,35,36,40].

This situation may worsen due to the health crisis of the disease pandemic caused by the coronavirus 2019 (COVID-19), since, during this period, health services and workers were mobilized to assist patients with COVID-19, aiming to avoid complications and fatal cases due to this disease. Thus, consultations, diagnostic tests and routine surgical procedures were postponed, impacting the evolution of clinical conditions, which aggravates the underlying disease and increases the need for more complex specialized care to contain the progress of these diseases[41]. Thus, there was a reduction in cancer diagnosis by the Unified Health System (SUS); comparing the period before and during the pandemic, it is estimated that about 15,000 new monthly cases were not identified, and a greater reduction in diagnosis was observed in the Northeast (-42.7%)[42].

CONCLUSION

The northeastern municipalities with the worst socioeconomic indicators related to education and health, measured by IFDM, had higher mortality rates due to CC between 2015 and 2019. Spatial clusters with high mortality rates were found in the states of Maranhão, Piauí, on the coast of Pernambuco, Alagoas, Sergipe, and Bahia. In addition, there was a maintenance of high mortality rates due to CC and a high percentage of death records classified as PNE, signaling the weaknesses of sus in enabling timely diagnosis and treatment.

With these considerations, it is necessary to evaluate the PNCC in these locations to identify the factors correlated with this reality, with regard to the gynecological preventive coverage, the evaluation of the quality indicators of this prevention program (collection, storage and reading of the slides), the referral for treatment of precursor lesions, and the time between diagnosis and the beginning of treatment.

CONTRIBUTIONS

All authors contributed substantially to the design and/or planning of the study; in the analysis and/or interpretation of the data; in the writing and/or critical review; and approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

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