Intra-urban spatial variability of breast and cervical cancer mortality in the city of São Paulo: analysis of associated factors

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ABSTRACT

Objective: To identify spatial variability of mortality from breast and cervical cancer and to assess factors associated in the city of São Paulo. Methods: Between 2009 and 2016, 10,124 deaths from breast cancer and 2,116 deaths from cervical cancer were recorded in the Mortality Information System among women aged 20 years and over. The records were geocoded by address of residence and grouped according to Primary Health Care coverage areas. A spatial regression modeling was put together using the Bayesian approach with a Besag-York-Mollie structure to verify the association of deaths with selected indicators. Results: Mortality rates from these types of cancer showed inverse spatial patterns. These variables were associated with breast cancer mortality: travel time between one and two hours to work (RR – relative risk: 0.97; 95%CI – credible interval: 0.93–1.00); women being the head of the household (RR 0.97; 95%CI 0.94–0.99) and deaths from breast cancer in private health institutions (RR 1.04; 95%CI 1.00–1.07). The following variables were associated with mortality from cervical cancer: travel time to work between half an hour and one hour (RR 0.92; 95%CI 0.87–0.98); per capita household income of up to 3 minimum wages (RR 1.27; 95%CI 1.18–1.37) and ratio of children under one year of age related to the female population aged 15 to 49 years (RR 1.09; 95%CI 1.01–1.18). Conclusion: The predicted RR for mortality from these cancers were calculated and associated with the socioeconomic conditions of the areas covered. Keywords: Breast neoplasm. Uterine cervical neoplasm. Mortality. Spatial regression.


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INTRODUCTION

Breast cancer (BC) and cervical cancer (CC) are serious public health problems worldwide. Regarding mortality, in 2020, BC was the leading cause of death from cancer among women, totaling 17,825 deaths, while CC ranked fourth with 6,627 deaths1.

However, BC and CC profiles are marked by their inverse nature, with the presence of higher BC incidence rates, but not mortality rates, in higher-income countries, and higher CC incidence and mortality rates in countries with lower levels of Human Development Index2.

The high rate of BC in highly developed countries is attributed to the higher prevalence of risk factors, such as late motherhood, nulliparity, non-breastfeeding or short-term breastfeeding, early age menarche, menopause at older ages, use of oral contraceptives and hormone replacement, alcohol intake, overweight, diet rich in processed foods and red meats, physical inactivity, work shifts, unemployment having worked before, exposure to ionizing radiation such as mammography and radiotherapy and to endocrine disrupting chemicals3-8.

As for CC, the main risk factor is persistent infection with the human papillomavirus (HPV), which is responsible for almost all cases of this cancer, and types 16 and 18 cause approximately 70% of all cases9. Given that the route of transmission of HPV is sexual10, the risk factors increase with difficulties in accessing prevention measures and the characteristics of one's sexual life (early start of sexual life, non-use of condoms, high number of sexual partners). Factors that help in the progression of infection to this cancer are high parity (>4 children), history of abortions, HIV immunosuppression, use of oral contraceptives, smoking, history of sexually transmitted infections (STIs), family history of CC, and menopause11-16. However, the knowledge on how geographic or temporal variations in morbidity and mortality from these types of cancer are related to specific etiological factors is still limited2.

For both BC and CC, there are well-designed preventive policies in place17,18; however, few studies have performed spatial data analysis19-21, especially at the intra-municipal level22. In the city of São Paulo, mortality from BC and CC show an inverse behavior, the former being more frequent in populations with better socioeconomic status, while the latter occurs in economically disadvantaged populations23. Because of the large municipal socioeconomic gradient, a spatial analysis of mortality from these diseases would make it possible to identify intra-urban spatial variability and associated factors, being an important tool to guide public policies.

METHODS

The city of São Paulo, capital of São Paulo State, is its largest, with estimated resident population in 2017 of 11,696,088 inhabitants, of which 6,135,970 (52.5%) are women24. It was divided into five Regional Health Coordinations and 25 Technical Health Supervisions and presented a territorial stratification (2015/2016 version) with 456 areas covered by Basic Health Units (BHUs), which are territories divided with the purpose of organizing the management of Primary Health Care25, as shown in Figure 1.

Between January 2009 and December 2016, the Mortality Information Improvement Program of the Mortality Information System (SIM/PRO-AIM) of the Epidemiology and Information Department, Municipal Health Department of São Paulo (CEInfo/SMS-SP), recorded 10,124 deaths from BC (10th Revision of the International Classification of Diseases — ICD-10: C50 to C50.9) and 2,116 deaths from CC (ICD-10: C53 to C53.9) in women aged 20 years and over in the city. These records were geocoded according to patients’ residence address, mainly through the Address Standardizer of the City of São Paulo. Addresses not found were geocoded by geolocation platforms that use Google Maps as a street database and by an application that has the Navteq26 street database.

BHU: Basic Health Unit; FHS: Family Health Strategy.

Source: GISA/CEInfo/SMS-SP (version 2015/2016).

Figure 1. Areas covered by Basic Health Units (2015/2016) in the city of São Paulo.
The conceptual theoretical models of factors associated with deaths from BC and CC were represented by Directed Acyclic Graphs (DAG) (Figure 2). Spatial regression models were adjusted to check for association of deaths from BC and CC (dependent variables) with social, demographic, economic, educational, and care indicators (independent variables) (Supplementary Material 1).

The digital grids of data of São Paulo’s coverage areas by BHUs were obtained from CEnInfo/SMS-SP, and the independent variables used in the spatial regression analysis were acquired from the Brazilian Institute of Geography and Statistics (IBGE), SIM/PRO-AIM, Information System of Cervical Cancer (SISCOLO), Breast Cancer Information System (SISMAMA), Outpatient Information System (SIA) and National Registry of Health Establishments System (SCNES). The independent variables, made available in polygons (Census Sectors or Weighting Areas) by the IBGE, were re-calculated for São Paulo’s coverage areas by BHUs using geographic operations, with the areas of these polygons considered as weights. The information provided by points (deaths and establishments) were aggregated into coverage areas through geographical intersection operation.

The number of deaths from BC and CC, grouped according to São Paulo’s coverage areas by BHUs, were modeled based on the Poisson probability distribution and through latent Bayesian Gaussian models26. Spatial autocorrelation was represented by structured and unstructured spatial random effects27, the Besag-York-Mollie model (BYM). The first one presents a conditional autoregressive (CAR) structure that smoothed the data based on the Queen-type contiguity neighborhood relation of order one. The second one is an independent and identically distributed random effect (iid) that modeled the uncorrelated noise. The BYM model was used with the proposed parameters28. The expected deaths from BC and CC were obtained, for all areas of coverage, by indirect standardization, based on specific rates by age groups. These values were considered in the modeling as offset, which made it possible to interpret the resulting coefficients as measures of relative risks (RR), having as parameters the mortality rates for the two cancers throughout the city during the study period for comparison.

Modeling was initially performed considering only intercepts and spatial random effects for each type of cancer. Before, however, an exploratory analysis was carried out to verify the existence of outliers and, when present, the independent variables were transformed by the cube root or logarithm (Supplementary Material 2). The independent variables were sorted into eight domains (Supplementary Material 3) and, for the ones presenting more than one variable, the independent variable that presented the lowest value based on the Deviance Information Criterion (DIC)29 was chosen in a bivariate modeling and considering spatial random effects.

With the set of independent variables for each condition, an exploratory analysis was carried out to assess collinearity through the variance inflation factor, considering values greater than or equal to 3 as cutoff point30. Then, a multiple regression modeling was performed, obtaining the posterior averages of RRs and respective 95% credible intervals (95%CI) adjusted for spatial autocorrelation29.

Modeling was performed using the Integrated Nested Laplace Approximation (INLA)31 approach. This is an efficient computational alternative to the Markov Chain Monte Carlo (MCMC) methods, especially when data has a spatial or space-temporal structure26. In the modeling, minimally informative priors were considered for fixed effects and priors with penalized complexity for random effects32. The analyses were performed in the R-INLA33 and INLAOut-puts34 packages of the R program34.

RESULTS

Of the total number of deaths from BC (10,124) and CC (2,116) registered, 10,066 (99.4%) and 2,101 (99.3%) were geocoded, respectively. The general rate of geocoding was 99.4%, and 92.1% of the records were geocoded at the exact point of the street and respective house number.

In Figure 3 shows the posterior averages of the RR predicted by the model for BC and the CC, obtained from the intercept modeling taking into account the structured and unstructured spatial random effects. Comparing the maps, both conditions presented opposite spatial patterns.

Mortality from BC in the city of São Paulo between 2009 and 2016, standardized by age group, showed a radial spatial pattern from the center of the city, that is, with higher predicted RR values in the central region, ranging from 1.03 to 1.16, and lower RR in peripheral regions, between 0.85 and 0.9. On the other hand, mortality from CC had higher values in peripheral regions, between 1.46 and 2.84, and lower values in the central region, from 0.40 to 0.84.

Table 1 shows the posterior means of RRs and respective 95%CI of each independent variable, adjusted for the spatial autocorrelation of mortality from BC and CC, respectively.

As to mortality from BC, three variables showed a statistically significant association. The “proportion (%) of employed people in the reference week with a usual time of commuting from work of more than one hour to two hours” and the “proportion (%) of women as head of the household” were negatively associated with the outcome. The variation of one standard deviation in these two variables corresponded to a 3% decrease in mortality. The variable “proportion (%) of deaths from BC in private health institutions” was positively associated with the outcome, and the variation of one standard deviation in this variable corresponded to a 4% increase in mortality.

As for CC mortality, three variables showed a statistically significant association. The variable “proportion (%) of employed people in the reference week with usual time of...
Figure 2. Conceptual theoretical models of factors associated with mortality from cervical and breast cancer represented by directed acyclic graphs.

**Caption:**
- **〇** Exposure
- **〇** Adjusted variable
- **〇** Unavailable variable
- **〇** Outcome

Prepared by: Study Group on Spatial Analysis (GEANES/FSP/USP).

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commuting to work from more than half an hour to one hour” had a negative association, and the variation of one standard deviation corresponded to an 8% decrease in mortality. The variables “household income (private household) per capita up to 3 minimum wages in July 2010”, “proportion (%) of deaths from cervical cancer that occurred in public health institutions/associated with the Unified Health System (SUS)”, “proportion (%) of employed people in the reference week with usual time of commuting for work from more than half an hour to one hour” had a negative association, and the variation of one standard deviation corresponded to an 8% decrease in mortality. The variables “household income (private household) per capita up to 3 minimum wages in July 2010” and “ratio (%) of children under one year of age related to the female population aged 15 to 49 years” showed a positive association. The variation of one standard deviation in

Table 1. Posterior means of spatial relative risks and credible intervals (95%CI) of factors associated with mortality from cervical and breast cancer in women aged 20 years and over, according to areas covered by Basic Health Units (2015/2016 version). City of São Paulo, 2009-2016.

<table>
<thead>
<tr>
<th>Factors</th>
<th>RR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion (%) of employed people in the reference week with usual time of commuting for work from more than 1 hour to 2 hours</td>
<td>0.97</td>
<td>(0.93–1.00)</td>
</tr>
<tr>
<td>Proportion (%) of women as head of the household</td>
<td>0.97</td>
<td>(0.94–0.99)</td>
</tr>
<tr>
<td>Ratio (%) of children under 1 year of age related to the female population aged 15 to 49 years</td>
<td>0.99</td>
<td>(0.96–1.02)</td>
</tr>
<tr>
<td>Proportion (%) of deaths from breast cancer occurring in private health institutions</td>
<td>1.04</td>
<td>(1.00–1.07)</td>
</tr>
<tr>
<td>Proportion (%) of employed people in the reference week with usual time of commuting for work from more than half an hour to 1 hour</td>
<td>0.92</td>
<td>(0.87–0.98)</td>
</tr>
<tr>
<td>Household income (private household) per capita up to 3 minimum wages in July 2010</td>
<td>1.27</td>
<td>(1.18–1.37)</td>
</tr>
<tr>
<td>Proportion (%) of women as head of the household</td>
<td>1.01</td>
<td>(0.96–1.07)</td>
</tr>
<tr>
<td>Ratio (%) of children under 1 year of age related to the female population aged 15 to 49 years</td>
<td>1.09</td>
<td>(1.01–1.18)</td>
</tr>
<tr>
<td>Proportion (%) of deaths from cervical cancer that occurred in public health institutions/associated with the Unified Health System (SUS)</td>
<td>0.98</td>
<td>(0.90–1.06)</td>
</tr>
</tbody>
</table>

RR: relative risk; CI: credible interval.

Figure 3. Posterior means of spatial relative risks of mortality from cervical cancer (A) and breast cancer (B) in women aged 20 years and over, according to areas covered by Basic Health Units. City of São Paulo, 2009 to 2016.
Mortality rates from breast cancer and cervical cancer showed opposite spatial patterns, associated with the socioeconomic conditions of the areas covered by BHUs in São Paulo. Regarding BC, the variables with a significant effect on mortality from this disease show that areas with a lower socioeconomic level have a lower risk of mortality from this cancer, while areas with a better socioeconomic level have a higher risk. Several studies discuss the positive association between mortality from BC and better socioeconomic levels. However, this indicator is also related to the incidence of cancer prevention programs. Considering that the vaccine is in fact effective, its result in the incidence or mortality of this cancer can only be verified in years or even decades.

The variables related to race/skin color were also not related to mortality from both cancer types; self-declared information, which is unfeasible at death, can generate bias when interpreting data collected. The illiteracy rate in the elderly population was also not associated with any of the diseases, probably due to the low proportion of illiterate elderly in the city of São Paulo — 5.9%. A study conducted in Paraná, Brazil, sought to spatially assess the socioeconomic disparities in access to health-related to mortality from BC and reported results that agree with ours. The authors explain that better socioeconomic conditions seem to be related to variables that influence mortality from this type of cancer. A high score of accessibility to oncology services (radiotherapy and chemotherapy) was positively correlated with mortality rates. Considering the incidence of BC, a spatial analysis with smoothed
incidence rates in the region of Iran, using spatial scanning statistics, showed that the incidence is a health problem in rich areas with higher levels of education and higher expenditures on health actions. Women living in these areas of better socioeconomic status were found to have higher expenditures on health care activities such as screening exams, resulting in a more frequent diagnosis of BC. In addition, they have easier access to cancer treatment centers and adjuvant therapies and are, therefore, likely to have better survival rates56.

However, American studies found a pattern of mortality from BC that differed from our findings. A national-scale study67 analyzed the geographic variation in incidence and mortality of female BC, detecting several significant spatial clusters that persisted even after adjusting for risk factors. Another study conducted in the United States58 evaluated geographic, racial and ethnic variations associated with mortality from BC among women living in 3,108 contiguous municipalities, from 2000 to 2015. Overall, mortality rates were higher in municipalities with high proportion of non-Hispanic black residents, low education and income, among others. However, the evaluation of the spatial variation of BC-specific mortality in Louisiana showed that higher mortality was associated with low income, worse socioeconomic status, poor access to and quality of health care, availability of fresh food, rurality and certain occupations in certain industries59.

With regard to CC, improving early detection and providing timely treatment is necessary to alleviate the burden of the disease. Population-based research in Costa Rica used data from the National Tumor Registry and assessed inequalities in the incidence of the disease. The results indicated a modest decrease in inequality between 1980 and 2010, given that the female population under 40 years of age had access to benefits from a national prevention program that was not experienced by the female population above this age group. Thus, CC cases dropped only among the youngest population, increasing the inequality in incidence60.

A study conducted in Baltimore evaluated the neighborhood correlation and spatial distribution of BC, CC, and colorectal cancer from 2000 to 2010 and found remarkable geographic variation by cancer type. CC was often diagnosed at younger ages when compared to BC, which was more impacted by the increasing age of residents61.

This study puts the spotlight on issues related to women’s health in a localized level, as it allows one to view the phenomenon according to areas covered by BHUs, a scale closer to reality.

**REFERENCES**


RESUMO

Objetivo: Identificar a variabilidade espacial da mortalidade por câncer de mama e colo do útero e avaliar fatores associados à mortalidade por esses cânceres no município de São Paulo. Métodos: Entre 2009 e 2016 foram registrados, no Sistema de Informações sobre Mortalidade, 10.124 óbitos por câncer de mama e 2.116 óbitos por câncer do colo do útero em mulheres com 20 anos e mais. Os registros foram geocodificados por endereço de residência e agregados segundo território adstrito. Foram realizadas modelagens de regressão espacial utilizando-se a abordagem bayesiana com estrutura de Besag-York-Mollèi para verificar a associação dos óbitos com indicadores selecionados. Resultados: As taxas de mortalidade por esses cânceres apresentaram padrões espaciais inversos. As variáveis associadas à mortalidade por câncer de mama foram: tempo de deslocamento para o trabalho entre uma e duas horas (risco relativo — RR 0,97; intervalo de credibilidade — IC95% 0,93–1,00); mulheres responsáveis pelo domicílio (RR 0,97; IC95% 0,94–0,99) e óbitos por câncer de mama ocorridos em estabelecimentos privados (RR 1,04; IC95% 1,00–1,07). À mortalidade por câncer do colo do útero, estiveram associados: tempo de deslocamento para o trabalho entre meia e uma hora (RR 0,92; IC95% 0,87–0,98); rendimento domiciliar até três salários-mínimos (RR 1,27; IC95% 1,18–1,37); e razão de menores de um ano em relação à população feminina de 15 a 49 anos (RR 1,09; IC95% 1,01–1,18). Conclusão: Foram calculados os RR preditos para a mortalidade por esses cânceres, que estiveram associados às condições socioeconômicas das áreas de abrangência. Palavras-chave: Câncer de mama. Câncer do colo do útero. Mortalidade. Regressão espacial.