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RESEARCH ARTICLE

Breast cancer in the Baixada Santista region and its relationship to contaminated areas

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Abstract

The aim of this study was to analyze the temporal distribution of breast cancer and its relationship with contaminated areas in the Baixada Santista metropolitan region, São Paulo. It is an ecological study on the distribution of breast cancer in the municipalities of the region as well as in regions exposed to environmental contaminants. The population consisted of women aged 20 years and over, totaling 3233 cases in the 12 years of the study. First, we calculated the total annual breast cancer coefficients by municipality, then we standardized by age and the indicator of contamination density by municipality. We then performed cartographic sequencing that revealed the evolution of outcome and exposure. The results showed that the municipality of Santos presented a higher coefficient of the disease. Pearson's correlation was positive with $r = 0.7$ at a significance level of $p = 0.036$. Spatially, the most contaminated areas presented higher breast cancer coefficients, except for the municipality of Peruíbe, which despite its low environmental contamination index, presented a high disease coefficient. This study confirmed the hypothesis that environmental contamination affects breast cancer distribution, and the temporal trend shows an increase in the disease in eight of the nine municipalities in the region.

Keywords Cancer · Breast cancer · Environmental contamination · Temporal analysis · Trend · Public health

Introduction

Breast cancer is the most common disease in women worldwide, with significant geographic variation of incidence, being higher in more developed regions (Ferlay et al. 2010; Trieu et al. 2015; Romaniuk et al. 2017). However, survival is higher in developed countries, likely due to the efficient screening and treatment of the disease (INCA 2015).

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In Brazil, for the years 2018 and 2019, it is estimated that 59,700 new cases of breast cancer were confirmed. This typology ranks first among the most incident cancer types in all regions of the country, except for the northern region where cancer of the cervix still predominates. Despite the wide variation of incidence in different regions of Brazil, the South and Southeast regions concentrate 70% of new cases, and in the State of São Paulo, where this study is located, it is estimated that standardized incidence rates for 2018 per 100 thousand women ranged from 54.37 to 68.78 (INCA 2018).

According to Villarreal-Garza et al. (2013), a possible reason for the increase in breast cancer is the combination of environmental, demographic, hereditary, and lifestyle factors. The onset and progression of the disease is multifactorial, including being older than 50 years old, however, some studies have observed increased disease in younger women before age 40 (Aguilla, et al. 2013; Villarreal-Garza et al. 2013; Donatus et al. 2014)), family history, hormonal factors, and 80 to 90% of breast cancer cases are associated with environmental contaminants present in workplaces, diet, social or cultural activities, as well as in the water, land, and air (INCA 2014).

The environmental contaminants with strong and medium evidence for breast cancer (CHE 2015) are estrogen/DES, ionizing radiation, ethanol, tobacco smoke (active and passive), aromatic amines, oryzaline, PAHS, PCBs, progestin, solvents, tetrachloroethylene, and with limited evidence, dichlorodiphenyltrichloroethane (DDT) and dioxins, among others (CHE 2015). However, in a remarkable review (Rodgers et al. 2018), it was found that a higher risk exists for exposures during breast development to DDT, dioxins, perfluorooctane sulfonamide (PFOSA), air pollution, PAHS, and occupational exposure to solvents and other agents such as components of gasoline. In occupational studies, various agents have been associated with breast cancer including exposure to carcinogens such as aromatic amines, ethylene oxide, artificial colorants and dyes, oil, and gasoline.

The Baixada Santista metropolitan region (BSMR) is located on the coast of the state of Sao Paulo and covers an area of 2419.93 km^2. It encompasses nine municipalities, i.e., Santos, Sao Vicente, Guaruja, Praia Grande, Cubatão, Itanhaém, Peruibe, Bertioga, and Mongaguá. The municipality of Santos is home to the largest port in Latin America, and the municipality of Cubatão is the largest industrial hub in the country (CETESB 2013). The region has several environmental contaminants in the soil, estuary, and air, and many of these contaminants are classified as carcinogenic. Worldwide, while several studies (Large and Wei 2017; Romaniuk et al. 2017; Peng et al. 2015; Brophy et al. 2012) suggest a possible association between breast cancer and environmental contamination, in the region, few investigations have been carried out (Faria et al. 1999; Zago et al. 2005) on cancer mortality or breast cancer mortality, respectively, both suggested association with environmental contamination.

This study analyzed the temporal distribution of breast cancer and its relationship with contaminated areas in the municipalities of the Baixada Santista metropolitan region.

Method

This is an ecological study in the BSMR between 2000 and 2011, with secondary data obtained from the Oncocentro Foundation of São Paulo (São Paulo Oncocenter foundation 2015 - FOSP) collected by municipality and year. Data on the population of at-risk women aged 20 and over were provided by the State Data Analysis System Foundation (SEADE 2015). Total breast cancer cases from 2000 to 2011 in the region in women over 20 years old totaled 3.233 cases.

Data on contaminated areas in each municipality of the Baixada Santista metropolitan region were obtained from the São Paulo State Environmental Agency (CETESB 2016), in addition to the number of areas by municipality and location. The agency is responsible for the development of control actions, licensing, supervision, and monitoring of potentially polluted activities. In this study, we considered all contaminants present in the municipalities reported by CETESB (2013)): Polycyclic aromatic hydrocarbons, metals, liquid fuels, aromatic solvents, halogenated solvents, polychlorinated biphenyls, phenols, biocides, phthalates, methane, total petroleum hydrocarbons (TPH), microbiological, dioxins and furans, radionuclides, and other inorganics.

First, we constructed the annual gross breast cancer coefficients for each municipality within the Baixada Santista metropolitan region (Bertioga, Cubatão, Guarujá, Sao Vicente, Itanhaem, Mongaguá, Santos, Peruíbe, and Praia Grande), according to the formula:

$$\frac{\text{diagnosed cases of breast cancer year } X \text{ in municipality } Y}{\text{population of at–risk women year } X \text{ in municipality } Y} * 10^n$$

Subsequently, we used the direct method for standardization and used the standard population aged 20 years or older from the State of São Paulo, Brazil, for the calculation. Disease coefficients when standardized or adjusted for age are necessary indicators for comparatively analyzing disease burden in particular regions. By adjusting the coefficients to an age standard, the risk-age factor is eliminated (Rouquayrol 1999).

To characterize the relationship between the number of contaminated areas in the municipality and the area of the municipality, a variable called contamination density was constructed that considers the number of contaminated areas in the municipality by the area of the municipality.

$$\text{ICA} = \frac{\text{number of contaminated areas in the municipality}}{\text{municipality area } X_i}$$

where X_i represented the municipalities of the MRBS (Bertioga, Santos, Guarujá, Cubatão, Praia Grande, Sao Vicente, Itanhaem, Mongaguá, Peruibe).

The degree of correlation between the variables (the breast cancer case coefficients and the exposure density indicator) was calculated using Pearson correlation (Callegari-Jacques 2003).

The cartographic measurements referring to Brazilian municipal and state boundaries were obtained from the Brazilian Institute of Geography and Statistics (IBGE 2012), which provides data in the 1:250,000 scale, using geographic projection and the SIRGAS 2000 Geodetic Reference System. In ArcGIS software (version 10.4), the polygonal vector files in the shapefile format referring to the Brazilian states and municipalities were introduced, and from them, the nine municipalities of the Baixada Santista metropolitan region were selected. Subsequently, the study area layer was georeferenced in the Universal Transverse Mercator (UTM) coordinate system, zone 23 south, maintained in the SIRGAS 2000 Geodetic Reference System.

In a GIS environment, the contamination and epidemiological cartographic data were integrated to be represented in a temporal cartographic sequencing that reveals the distribution and spatiotemporal evolution of breast cancer rates in BSMR municipalities. In the 12 maps that compose the temporal cartographic sequencing, the breast cancer occurrence data were spatialized into point features generated in the ArcGIS software (Spatial Statistics Tools module) from the center of each municipal polygon. Varied sizes and colors were chosen, respecting the thematic representation, in which a strong or weak value translates into a strong or weak signal, respectively. For the representation of the environmental contamination indices, the calculated indices were used and spatialized within the municipal polygons. The organization and representation of the data as well as the creation of the maps that make up the temporal cartographic sequencing were performed in the ArcGIS software.

For trend analysis, we used the linear regression model ($Y = a + bxi$), where Y represents the year, x is the breast cancer rate, and we used a determined equation for each municipality; several models were tested and the most appropriate was the one that presented the highest explanation coefficient. Therefore, for each municipality we present an explanatory model as follows: (Bertioga, year = 2010.01 + 0.659 coef; Cubatão, year = 2002.515 + 0.325 coef; Guaruja, year = 1999.508 + 0.381 coef; Itanhaém, year = 2003.107 + 0.339 coef; Mongaguá, year = 2003.253 + 0.314 coef; Peruíbe, year = 2000.114 + 0.462 coef; Praia Grande, year = 2000.078 + 0.401 coef; Santos, year = 1996.428 + 0.571 coef; São Vicente, year = 2000.777 + 0.351 coef). Statistical Package for Social Sciences, version 15.0 (SPSS) and Statistics for Windows 8.0 were used for analysis.

Results

Table 1 presents the standardized breast cancer coefficients by year and municipality of the Baixada Santista metropolitan region. The municipality of Santos presented the highest breast cancer coefficients, followed by Peruíbe, Guarujá, Praia Grande, Sao Vicente, Cubatão, Mongaguá, Itanhaém, and Bertioga.

Table 2 presents the breast cancer coefficients from 2000 to 2011 and the environmental contamination index for each municipality.

The municipalities with the highest breast cancer coefficients also had the highest environmental contamination index, as shown in Table 2, except for the municipality of Peruíbe, which despite low contamination, showed high rates of the disease.

A positive correlation was observed between the environmental contamination index and the breast cancer coefficient $r = 0.7$; $p = 0.036$.

Figure 1 shows the trend analysis of breast cancer for the nine municipalities of the region and shows an increasing trend for all municipalities, except for the municipality of Bertioga which presents a decreasing trend of the disease.

The spatial distribution was composed using cartographic sequencing of the 12 years of the study. Outcome (breast cancer coefficient) and exposure (environmental contamination) data were spatialized by year and for each municipality of the BSMR (Fig. 2). Temporal cartographic sequencing reveals the distribution and spatiotemporal evolution of breast cancer coefficients in the municipalities.

The highest coefficients of the disease were the municipality of Santos, followed by the municipalities of Peruíbe, Guarujá, Praia Grande, Sao Vicente, Cubatão, Mongaguá, Itanhaém, and Bertioga. It was also identified in the study that the municipalities that presented the highest contamination rates presented the highest breast cancer coefficients, except for the municipality of Peruíbe, which despite having a low contamination index, presented a relatively high disease coefficient over the last 8 years.

Table 1 Standardized breast cancer coefficients per year/100 thousand women in the Baixada Santista metropolitan region, São Paulo, from 2000 to 2011

Municipalities	Year											
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Bertioga	32.18	31.78	36.87	0.00	13.52	12.19	9.29	0.00	15.64	24.27	0.00	11.89
Cubatão	16.78	41.82	48.92	27.19	34.74	24.63	25.13	39.19	18.84	65.65	40.92	42.12
Guarujá	30.04	31.51	38.54	41.88	44.72	33.29	30.73	34.14	58.35	51.63	42.84	32.78
Itanhaém	8.78	26.86	26.33	35.85	16.61	21.55	6.05	20.11	37.30	53.56	24.60	24.52
Mongaguá	46.36	18.75	35.24	10.53	30.75	35.70	26.60	13.98	37.82	75.43	42.18	33.26
Peruíbe	18.09	40.67	50.38	45.99	26.85	41.01	24.02	33.61	53.59	55.48	54.36	41.62
Praia Grande	36.61	28.76	38.68	37.69	46.77	37.79	30.92	21.25	35.64	61.88	44.98	47.23
Santos	35.97	49.97	67.65	74.29	68.15	82.53	46.52	56.91	72.76	68.03	73.70	84.12
São Vicente	18.44	22.46	39.99	46.63	47.83	42.22	28.64	29.85	45.41	43.26	40.39	33.21

Table 2 Breast cancer coefficients and environmental contamination index in the BSMR from 2000 to 2011

Municipality	Breast cancer coefficient	Contamination index
Santos	65.05	0.30
Cubatão	35.50	0.27
Guarujá	39.20	0.20
Praia Grande	39.02	0.20
São Vicente	36.53	0.16
Mongaguá	33.88	0.03
Itanhaém	25.18	0.02
Peruíbe	40.47	0.02
Bertioga	15.64	0.01

Discussion

In the Baixada Santista metropolitan region, the municipality of Santos presented the highest breast cancer coefficients, followed by the municipalities of Peruíbe, Guaruja, Praia Grande, Sao Vicente, Cubatão, Mongaguá, Itanhaém, and Bertioga.

The linear regression model between the standardized breast cancer coefficients and the environmental contamination density in the region showed that the higher the environmental contamination, the higher the disease coefficients.

In the trend analysis, the data showed that in eight municipalities of the BSMR, there was a tendency for the disease to increase, except in the municipality of Bertioga which showed a decreasing trend.

The municipality of Santos presented standardized breast cancer coefficients with significant differences from other municipalities in the region. It is worth mentioning that several factors can contribute to the increase of the disease, such as advanced age, genetic, hormonal factors, and especially environmental factors. The presence of environmental contamination in the region may be a major factor in the high increase in breast cancer rates, as suggested in previous studies.

In the context of breast cancer, it is possible to observe variations in the distribution of the disease by country, state, and municipality. This is shown in several studies worldwide, such as a 2008 to 2012 temporal study (Fei et al. 2016) which showed a stable incidence throughout the period, with areas of low incidence showing a growing trend, while areas with high incidence showing no variation.

In the study (Habib et al. 2016) from 2005 to 2012, there was a modest increase in distribution and the rate of 34.9/100 thousand was considered especially high for the region. A spatio-temporal study (Zhou et al. 2015) between 2007 and 2012 showed rapid growth between 2007 and 2010 and a leveling-off between 2010 and 2012. The authors of this study attributed this trend to environmental, socioeconomic, and genetic factors.

These studies contrast with those found in the BSMR, which have higher coefficients and a growth trend in eight of the nine municipalities in the region.

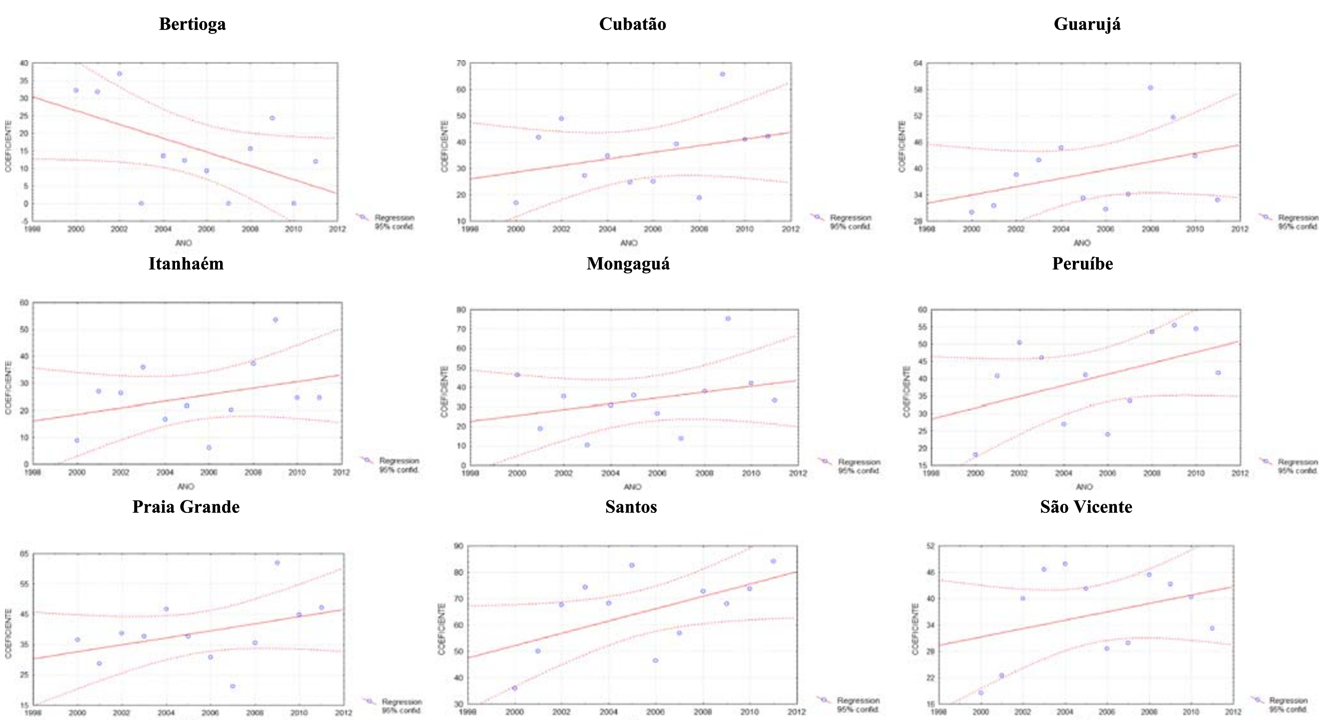

Fig. 1 BSMR municipal trend graphs

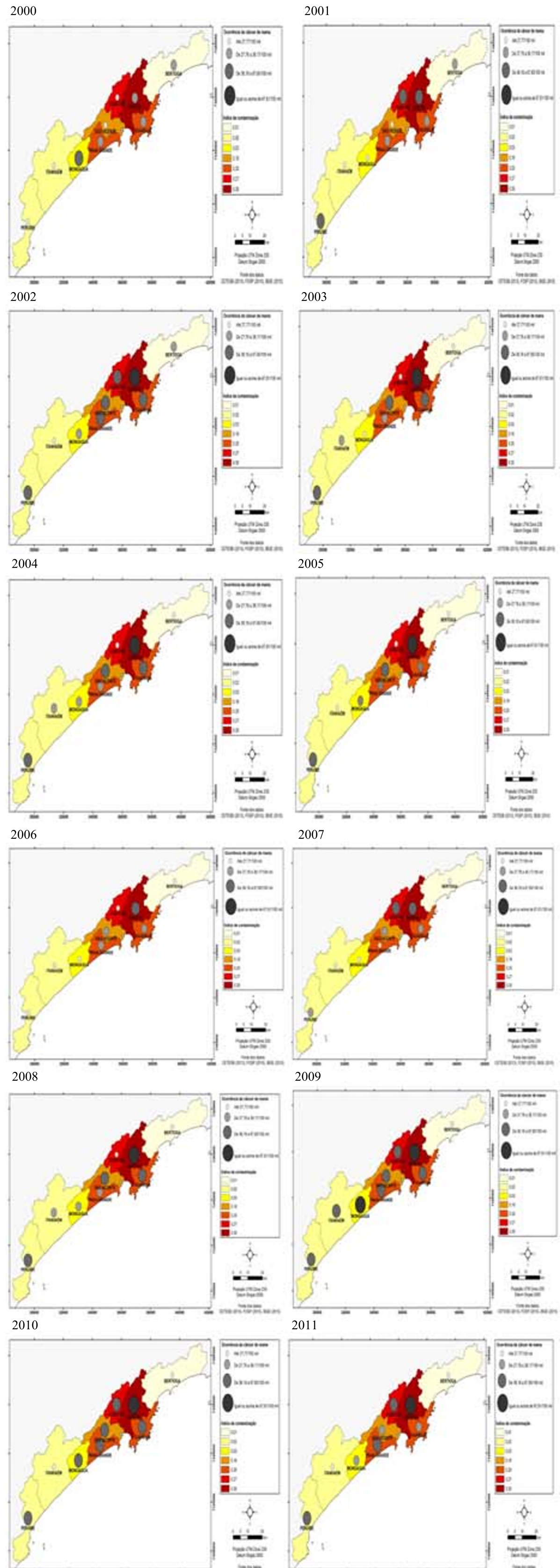

Fig. 2 Maps of relationship between the occurrence of breast cancer and the environmental contamination index in BSMR between 2000 and 2011

In addition to geographic variations related to breast cancer, other important factors found in several studies should be considered such as access to health services, coverage of specific exams such as mammography, and the speed and quality of treatment that interfere with the distribution of the disease and compromise the patient's treatment and survival (Gebrim and Quadros 2006; Trufelli, et al. 2008; Oliveira et al. 2011; Renck et al. 2014). A delay in diagnosis and treatment of the disease can reach 142.5 days in Brazil, 2.4 times longer than recommended according to Law No. 12,732 which is 60 days (Trufelli, et al. 2008; Almeida 2015; Souza et al. 2015; Traldi et al. 2016). In Germany, after the introduction of the mammographic examination, advanced breast cancers decreased and the incidence of the disease increased, showing that the disease was detected in younger age groups (Simbrich et al. 2016). Although not analyzed in this study, in Brazil, mammographic coverage according to the last release of data in 2013 was 60%, with important regional differences (North, 38.7%; Northeast, 47.9%; Southeast, 67.9%; South, 64.5%; and Midwest, 55.6%) in women utilizing the Unified Health System (SUS), aged 50 to 69 (IBGE 2014), which is below the 70% recommended by the WHO.

The municipalities with the highest environmental contamination index had the highest breast cancer coefficients, except for the municipality of Peruíbe, which despite low contamination had high rates of the disease, which may be related to a diffuse contamination in the region, different from other municipalities where there are deposits of contaminated materials.

While this study did not analyze specific contaminants, several studies conducted in other countries have shown an association between breast cancer and environmental contamination. One study (Dai and Oyana 2008) identified an association between very high levels of breast cancer in areas with dioxin-contaminated soil (Brophy et al. 2012), which supports the hypothesis of an association between breast cancer and exposure to carcinogens and endocrine disruptors. In this case, the high risk included agriculture, automotive plastic manufacturing, canning, and metalworking.

An ecological study (Large and Wei 2017), which analyzed the relationship between PAHs and breast cancer incidence, suggests a potential relationship between atmospheric emission of PAHs and the geographic variation of breast cancer incidence in the northeast and southeast of the USA. The northeast, where they found an increased incidence of breast cancer, is more industrialized and polluted than the southeast.

A case-control study, developed in China (Peng et al. 2015) on breast cancer risk from cadmium exposure, showed that cadmium concentration was significantly higher in the blood of breast cancer patients compared with controls, and that high cadmium concentrations were observed in patients in the advanced stages of the disease, suggesting that cadmium may favor the onset of breast cancer.

Other studies have also shown that living near or in a contaminated area is an important risk factor for developing breast cancer (Dai and Oyana 2008; Vieira et al. 2008).

Although studies suggest that environmental contaminants have favored an increased incidence of breast cancer, we had difficulty comparing our results since available studies analyzed specific contaminants, which was not possible in this study.

We concluded that the temporal distribution of breast cancer in the 12-year series was higher in the municipality of Santos, followed by Peruíbe, Guarujá, Praia Grande, Sao Vicente, Cubatão, Mongaguá, Itanhaém, and Bertioga. In the spatial distribution, the lowest coefficients were found in the city of Bertioga which also presented the lowest index of environmental contamination. The highest coefficients were identified in the areas with the highest environmental contamination index, except in the city of Peruíbe, which despite low contamination, presented high disease coefficients. This study confirmed the hypothesis that environmental contamination alters the distribution of breast cancer, and that in eight of the nine municipalities in the region, the tendency is for the disease to increase.

Although data from the best source of hospital records available in the state of São Paulo were used, there may be information bias due to underreporting. Data came from a variety of sources, which may compromise the quality of the information. However, this cannot be considered a differential bias because, if it does exist, it may be leading to underreporting of the effect. Other risk factors were not included in the study, however, the result portrays the reality of a region and draws the authorities' attention to the risk of breast cancer related to exposure to environmental contamination. From this study, we identified the need for further investigations in the region with new designs especially of specific contaminants.

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