

Higher prevalence of breast cancer in cities with higher Human Development Index: an epidemiological study at Cancer Hospital of Muriaé-MG Larissa Bonato Bertoni Murta Silva^{1*}, Sergio Gomes da Silva², Carla Simone Freitas³, Mauricio Alexander de Moura Ferreira⁴, Erica Mangaravite⁵.

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Abstract

Introduction: Cancer is the second most common cause of death. In the context of mortality in ageing populations, breast cancer receives attention as it affects women over 50 years old.

Objective: Here, we use hospital cancer records to evaluate the epidemiological and demographic profile of women with breast cancer attempted at Cancer Hospital of Muriaé.

Methods: Based on medical records, we compared the city and/or microregion of the patient with breast cancer at the Cancer Hospital of Muriaé of the Cristiano Varella Foundation, in Muriaé, Minas Gerais, Brazil, from 2016 to 2018.

Results: The 1536 patients with breast cancer exhibited a median age of 54 years old. The majority of the patients - more than 90% - come from the state of Minas Gerais, with others coming from southeastern states. Of the 10 most prevalent cities (140 cities were sampled), Muriaé is the first, and most of them have as main GDP (Gross Dosmetic Product) source industrial activity and other services (tertiary sector). The higher the municipal Human Development Index (HDI-M), the higher was the number of breast cancer cases (positive and significant correlation).

Conclusion: Thus, breast cancer does not have a single preventive action, and preventive policies need to be implemented in order to be more effective in the most prevalent areas.

Keywords: Healthy City; epidemiology; Primary Prevention; GDP

Introduction

In Brazil, cancer is the second most common cause of death and it is the biggest cause of death in 516 Brazilian cities, of which 84 are located in the state of Minas Gerais [1]. Projections indicate the occurrence of 26 million new cancer cases and 17 million cancer deaths worldwide, by the year 2030. These projected numbers are explained by the demographic growth and the ageing of the population, especially in the less developed regions. [2]. Some authors assume that in the next decades, mortality

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from malignant neoplasms will overcome death from chronic non-communicable diseases [3].

In the context of ageing, breast cancer is, together with chronic non-communicable diseases, one of the biggest challenges for the Ministry of Health, in Brazil. Breast cancer most affects patients over 50 years old, and its prevalence increases with age, being uncommon before 35 years of age [4]. The mortality rate of women under 40 is 10 deaths per 100,000 women [5]. This is the type of cancer that mostly affects women in Brazil (excluding non-melanoma skin tumours) and exhibited 13.22 deaths per 100,000 women (totalling 626,679 deaths in 2017) [6]. South and Southeast regions have the highest rates, with 14.14 and 14.10 deaths per 100,000 women in 2017, respectively [6].

Diagnosis of breast cancer patients in more advanced stages worsens the prognosis, and it is related to difficulties in accessing suitable diagnostic methods and proper treatment. The disease is multifactorial, which can be linked to lifestyle such as obesity (or overweight); sedentary lifestyle; consumption of alcoholic beverages; frequent exposure to ionizing radiation; hormonal factors such as first menstruation before age 12; nulliparity; first pregnancy after 30 years; not breastfeeding; menopause after 55 years and post-menopausal hormone replacement [4]. Another risk factor is the inheritance of genetic mutations, which correspond to 5% to 10% of all cases. Changes in genes, such as BRCA, increase the possibility of developing the disease [7].

Due to this continued growth, information such as prevalence is essential for cancer control programs, both nationally and regionally [8]. Population-based cancer registries, hospital cancer registries and mortality information are the basis for the development of more efficient prevention strategies [6]. The Cancer Hospital of Muriaé (HCM, Hospital do Câncer de Muriaé) is the largest oncology complex of Minas Gerais, has a high complexity centre in oncology. It serves 270 municipalities in the Mata Mineira Zone and the surrounding areas and performs 84% of the visits through the Brazilian Unified Health System (SUS, Sistema Único de Saúde), with a coverage of approximately 7 million inhabitants [9].

Thus, the city of origin of the patients (or the micro-region) was related to breast cancer prevalence at the HCM of the Cristiano Varella Foundation, in Muriaé, Minas Gerais, from 2016 to 2018. In addition, the specific objectives were to address the following questions: (1) What is the epidemiological and demographic profile of the patient with breast cancer attempted at HCM? (2) Is there a relationship between the socioeconomic characteristics of the city and the number of breast cancer cases? (3) Is there a local factor (local agriculture, industry, etc.) that could be related to this prevalence of breast cancer? Also, alternatives for improving prevention strategies were discussed to collaborate with the reduction of breast cancer cases.

Material and Methods

This is an epidemiological, descriptive and observational study. The population was limited to patients who underwent cancer treatments at the HCM of the Cristiano Varella Foundation. This study was approved by the ethics and research committee of UNIFAMINAS and by Plataforma Brasil (number: 3,356,559 and CAAE: 13603719.7.0000.5102). Data were extracted from pre-existing medical records from 2016 to 2018. The sample was selected by the number of the International Classification of Diseases (ICD, **Table 1**) that corresponded to breast cancers. In addition to the ICD, information of age, sex, city and state was collected from each patient. The personal address, however, was not accessed in order to minimize risks related to patient privacy. Descriptive analyzes (median, minimum and maximum) were performed with the age of the patients and also compared between the cities with the highest prevalence of breast cancer.

A total of 1536 medical records were collected, in which socioeconomic information for each city (HDI-M, education, population size, GDP- Gross Domestic Product, and per capita income) was obtained from the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística - IBGE) [10]. In addition, information about the presence of industries and/or agriculture in cities was obtained. Finally, the geographic distance from each city to the HCM was also counted. Statistical analyses were performed in the RBio version [119, 11]. Kolmogorov-Smirnov test was used to verify the normality of the data [11]. After confirming the normality (p-value <0.05), Pearson's correlation was performed between each characteristic of the 140 cities and the number of cases of breast cancer in each city. The results were considered significant at 5% probability (p-value <0.05).

Table 1. International Classification of Diseases (ICD) code anddescription, and the number of patients sampled (N).

ICD code	ICD Description	Ν
C500	Malignant neoplasm of nipple and areola	2
C501	Malignant neoplasm of central portion of breast	3
C502	Malignant neoplasm of upper-inner quadrant of breast	4
C503	Malignant neoplasm of lower-inner quadrant of breast	0
C504	Malignant neoplasm of upper-outer quadrant of breast	4
C505	Malignant neoplasm of lower-outer quadrant of breast	1
C506	Malignant neoplasm of axillary tail of breast	99
C508	Malignant neoplasm of overlapping sites of breast	934
C509	Malignant neoplasm of breast of unspecified site	489

Results

The number of patients with breast cancer was 1536 between 2016 and 2018 in HCM. Only four patients were male. Patients with breast cancer represented 13.52% out of all patients in this period (11,361). Malignant neoplasm with invasive lesion was the most frequent (n = 934), followed by unspecified malignant breast neoplasm (n = 489) (Table 1). The median age was 54 years old, the youngest and oldest patients were 17 and 98 years old, respectively (Figure 1). Among the ten most frequent cities, some differences in median age were observed, and they varied from 51 to 60 years old (Figure 2).

Most patients were from the state of Minas Gerais (Figure 3).One hundred and forty cities were sampled. Out of them, 33 cities

exhibited only one patient each (Supplementary **Table 1**). The state with the highest number of cities mentioned by the patients was Minas Gerais (112 cities), followed by Rio de Janeiro (23 cities), Espírito Santo (4 cities), and São Paulo (1 city). Similarly, the state of Minas Gerais was the most frequent in the number of patients (1398 patients), followed by Rio de Janeiro (128 patients), Espírito Santo (8 patients), and São Paulo (1 patient). In Minas Gerais, the city of Muriaé was mentioned by 256 patients (Supplementary **Table 1**, **Figure 3**). The ten cities with the most frequent number of patients are shown in **figure 2**.



Figure 1. Number of patients per age with breast cancer from 2016 and 2018 in HCM



Figure 2. Number of cases and median age of patients in the cities with the highest number of cases.

In the correlation analysis between the number of cases and the socioeconomic characteristics of the city, only two characteristics were significant: one positive, between the HDI-M and the number of cases (r = 0.27, p-value <0.01) and, another negative, between distance to Muriaé-MG and number of cases (r = -0.18, p-value <0.03). Both values revealed a weak correlation. In fact, the most frequent cities were closer to Muriaé (Figure 3). The most distant city of Muriaé was Jaíba-MG, 931.6 km from Muriaé, and the closest was Patrocinio do Muriaé-MG, 24.6 km

(Supplementary Table 1).

Out of the ten most frequent cities according to the number of patients (Figure 2), nine were from the state of Minas Gerais, in which seven were in Mata Mineira Zone. This mesoregion brings together 217 million inhabitants, representing 11.1% of the population of Minas Gerais. It is responsible for 7.6% of Minas Gerais GDP, having the service sector as the main source (68.4%), following industry (22.6%) and agriculture (9.0%) [9]. Bom Jesus do Itabapoana was the only city of the ten most frequent in the study that belonged to the state of Rio de Janeiro, located 91.6 km from Muriaé. The main source of its GDP is industry and other services [10]. This city belongs to the Northwest region in the state of Rio de Janeiro and exhibited 11.1% of the entire population of its region (this region represents 2% of the state of Rio de Janeiro). Trade in the Northwest region constitutes 43.5% of GDP, while industries 11.4% and agriculture 4.0% [11]. As well as Muriaé-MG and Bom Jesus do Itabapoana-RJ, the cities Além Paraíba-MG (71 patients), Cataguases-MG (47 patients), Leopoldina-MG (44 patients), Caratinga-MG (44 patients), Carangola-MG (41 patients), Uba by Ubá-MG (35 patients) have industries and other services (tertiary sector) as its main source of GDP.



Figure 3. Map of the Southeast region of Brazil with the location of the cities prevalent for breast cancer in the years 2016 and 2018. The legend with the colour gradient indicates the number of cases per city.

Manhuaçu-MG was the second most frequent city (80 cases), the industrial sector and other services are the main sources for the municipality's GDP [13]. The industrial park of Manhuaçu consists mainly of food, agricultural machinery, concrete, and metallurgy industries. In addition, Manhuaçu has 27.51% of people working in the agricultural sector, 15.12% in industry, 17.35% in commerce and 35% in the services sector [15]. Mutum-MG was the third most frequent city (51 patients). It is the only city among the top ten that still has agriculture as one of the main sources of GDP, with coffee and livestock (cattle and chickens) as main sources [16]. The GDP of Mutum was the lowest of the ten most prevalent cities [16].

Discussion

In this study, the number of breast cancer cases between 2016 and 2018 at HCM were described and evaluated regarding the patient's city of origin. The number of cases showed a weak positive correlation with the HDI-M of each patient's city of origin. The prevalence of breast cancer represented 13.52% (out of 11,361 patients) within the cases from HCM and was higher in relation to lung, prostate, colon and rectum cancer, and cervix in HCM (data not shown).

Four men (out of 1,535) were affected by breast cancer (0.26% of cases), in the same period. Men do not have a developed breast as women have, however, they do have breast tissue thus, being conducive to developing cancer in this location [6]. This neoplasm in men is rare, representing only 1% of the total cases of the disease in Brazil[17]. Breast cancer in men may be related to gene mutations (*BRCA1 and BRCA2*), Klinefelter syndrome, liver disease, obesity and it can also affect patients who have undergone radiotherapy in the chest area[6]. Regarding the age of the patients, the median of this study (54 years) was similar to the national median, with the most prevalent age group between 50 and 59 years[2,18].

The Southeast Region is the second largest in Brazil in terms of the incidence of new cancer cases, behind the South Region [19]. At HCM, 1398 patients with breast cancer were treated between 2016 and 2018, with Minas Gerais being the most frequent state among the patients under study. Minas Gerais has 37 Hospitals/ Clinics with the capacity to carry out oncological treatments [6]. Within 100 km from Muriaé, there is a hospital specialized in cancer, located in the city of Cataguases-MG. The State of Rio de Janeiro has 30 Hospitals/Clinics with capacity in this segment, located in Itaperuna [6] within 100 km radius from Muriaé. Thus, HCM, located in the mesoregion of Mata Mineira Zone has a strategic and important location that allows the care of patients from many cities in the surrounding area.

Muriaé had a higher number of cases (n = 256), which can be explained by the fact that HCM is located in this city, and therefore, easier to access. This facility may have been reflected in the correlation between distance to Muriaé and the number of cases being negative and significant, although weak. However, this higher number of cases compared to other cities may have been a bias in this study. Patients from other cities are allowed to take cancer treatments at HCM, the registration can be carried out by proof of residence of any person, which allows patients to provide the address of friends or family members residing in Muriaé.

The number of breast cancer cases per city and HDI-M showed a positive and significant correlation, yet weak. This indicates that the higher this index (HDI-M), the greater the number of breast cancer cases. Although treatment and the chance of cure are higher in developed countries, a higher prevalence of cancer has been observed in places with high rates of human development [20]. The calculation for HDI-M considers three important dimensions: 1) the opportunity to live a far and healthy life; 2) have access to knowledge; 3) have a standard of living that guarantees basic needs. However, identifying this correlation gives insights that the health and longevity criteria are not adequate in the calculation and they should be revised.

The Brazilian population experience an epidemiological transition in which the number of breast cancer cases has surpassed the number of cervix cancer. This profile occurs in developed countries such as Norway and Australia, for example [20]. Urbanization and increased consumption of processed foods are likely related to the increase in the prevalence number of breast cancer in Brazil [21]. Consumption of processed foods in the country has increased in the past years. According to INCA, industrialized foods should be avoided, eating more fresh foods, especially of plant origin, or minimally processed foods contribute to health and reduce cancer risk factors [22]. This finding suggests that the disclosure of information about healthier eating habits is also not widespread. Thus, the item "access to knowledge" of the HDI-M calculation should be revised.

Muriaé has strong commercial and industrial growth [16]. It is the 4th largest textile centre in Minas Gerais, having 750 companies in this main sector. Industries producing food and beverages and assembling vehicles are also very important [23]. The main industries located at Bom Jesus do Itabapoana (RJ) are: steel products, textiles and industrial machinery. Textile industry workers manipulate dyes containing amines that can be carcinogenic [24]. Ministry of Health reports that industries such as rubber, plastics, chemicals, oil refineries and PVC manufactures are the main cancer propensities [25]. However, studies involving cancer breast and industries are scarce.

In Manhuacu (second largest number of cases) and Mutum, with their important agricultural coffee production, it is possible to highlight the presence of pesticides [26]. Coffee crops are perennial plants that are treated, throughout the year, with fertilizers and applications of pesticides against pests [26]. Even if this is not the main economic activity in the state, it is an activity of great importance [27]. The mesoregion of Mata Mineira Zone is the second-largest producer of coffee and the third-largest producer of rice in the state [13]. The overuse of pesticides is directly related to the incidence of cancer [28]. Cities such as Guaíra-SP and Nova Ubiratā-MT are the first and third-largest agricultural producers in Brazil, respectively, and they are included in the 516 cities in Brazil in which cancer is the main cause of deaths [1,29]. Brazil is the country with the highest consumption of these toxic products since 2008, producing 250 thousand tons of pesticides per year [30]. Exposure to pesticides is chronic, affecting producers, people living in rural areas, residents of nearby areas and people in the urban environment (consumption of contaminated food) [30]. Women should avoid exposure to chemicals and pesticides, as this is one of the few preventive measures to reduce the risk of developing breast cancer [31].

In the control of breast cancer, prevention and early detection should be prioritized [32]. Preventive policies are necessary to make the population aware of the required cancer care and prevention. HCM provides prevention campaigns in many cities in the region, where the population can perform mammography and be instructed on how to perform the breast touch exam. Besides, it also organizes events, such as walks, intending to alert and raise awareness about the prevention of breast cancer [9]. Reinforcing these campaigns and raising their frequencies to the most prevalent cities is important to manage early diagnosis in time to receive efficient treatment.

Primary prevention of breast cancer is important and includes approaches related to lifestyle. Consumption of fruits and vegetables is significantly associated with a lower risk of breast cancer [33]. Analysis with 16 studies showed that an increase of 10 g/day in fibre intake results in a 5% lower risk of breast cancer [33]. Secondary prevention is the monthly breast self-exam and mammography [34]. In most cases of breast cancer in the world, patients have no family history of the disease (80%), with only 5 to 10% of cancer breast cancer attributed to genetic mutations, 50% of the cases attributed to the main risk factors[32]. Thus, the Government should well inform women that they should adopt healthier habits, as well as carry out periodic examinations and observe their body and the changes that may occur in it.

Conclusions

Since higher HDI-M correlated to a higher prevalence of breast cancer, there is an indication that health and longevity criteria are not adequate in the calculation of HDI-M and they should be revised. Also, studies relating cities of patients to types of cancer are not usual, and this highlights the importance of this study as a source of information for new prevention strategies. Finally, breast cancer does not have a single prevention and preventive policies must be worked out to be more effective, particularly in higher prevalence areas. In Brazil, this is not the reality yet, as breast cancer is the one that most affects and leads to deaths of Brazilian women.

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