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Clinical characteristics and spatial analysis of breast cancer in Jalisco, Mexico

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Abstract

Background: *A study that involved spatial analysis tools is presented to demonstrate their possible impact on secondary prevention actions of breast cancer (BC).* **Objective:** *To examine clinical characteristics of BC in women living in Jalisco, Mexico, and to analyze the spatial distribution of diagnoses.* **Methods:** *Ecological-exploratory study. Clinical records of women diagnosed with BC during 2013-2017 were reviewed to collect clinical and sociodemographic variables. Using descriptive, inferential, and spatial statistics, age groups were compared according to stage classification (early/late), and spatial density.* **Results:** *There were 1,245 diagnoses. Average age 52.9 years (± 12.3); 80.7% performed housework. According to mammography, 55.7% of women reported BI-RADS 4 and 5; 55.2% were diagnosed late, mainly in the ≥ 60 age group (odds ratio = 1.15, 95% confidence interval = 0.65-1.09). 87.5% of diagnoses were concentrated in municipalities with higher population density in the study area; a higher number of diagnoses per spatial unit (km^2) were observed in the northeast area.* **Conclusions:** *BC detection and diagnosis are still performed in clinically advanced stages, so it´s suggested to focus secondary prevention actions territorially to increase their population impact.*

Keywords: *Breast neoplasms. Early detection of cancer. Biomarkers tumor. Spatial analysis. Geographic mapping.*

Características clínicas y análisis espacial del cáncer de mama en Jalisco, México

Resumen

Antecedentes: *Se presenta un estudio que involucró herramientas de análisis espacial para demostrar su posible impacto en acciones de prevención secundaria para cáncer de mama (CM).* **Objetivos:** *Examinar características clínicas del CM en mujeres residentes de Jalisco, México, y analizar la distribución espacial de los diagnósticos.* **Métodos:** *Estudio ecológico-exploratorio. Se revisaron expedientes clínicos de mujeres con diagnóstico de CM del periodo 2013-2017, se recolectaron variables clínicas y sociodemográficas. Mediante estadística descriptiva, inferencial y espacial se compararon grupos de edad según clasificación del estadio (temprano/tardío) y la densidad espacial.* **Resultados:** *Se hallaron 1,245 diagnósticos. Edad promedio 52.9 años (± 12.3). El 80.7% realizaba labores domésticas. Según mastografía, el 55.7% de las mujeres reportó BI-RADS 4 y 5; el 55.2% fueron diagnosticadas tardíamente, principalmente en el grupo de 60 o más años (OR: 1.15; IC 95%: 0.65-1.09). El 87.5% de los diagnósticos se concentró en municipios con mayor densidad poblacional en*

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el área de estudio; se observó un mayor número de diagnósticos por unidad espacial (km²) en zona noreste. **Conclusión:** *La detección y diagnóstico de CM aún se realiza en etapas clínicamente avanzadas, por lo que se sugiere focalizar territorialmente acciones de prevención secundaria a fin de aumentar su impacto poblacional.*

Palabras clave: *Neoplasias de mama. Detección temprana de cáncer. Biomarcadores tumorales. Análisis espacial. Mapeo geográfico.*

Introduction

Worldwide, breast cancer (BC) not only represents one of the most common cancers but also the main cause of mortality for women[1,2]. Mortality rates have shown a sustained increase in the past two decades[3], mainly in low- and middle-income countries[4]. Similarly, in Mexico BC has posed a health issue for women, especially in the reproductive or advanced stage of life. In 2020, BC represented 15.3% of all malignant neoplasms among women in Mexico, with a mortality rate of 17.9/100 thousand women over 20 years of age[5,6].

In this sense, early clinical diagnosis has proven to be one of the most effective secondary prevention measures to timely address BC[7]. Moreover, it is considered one of the most important prognostic criteria for survival along with some biomarkers, such as estrogen receptors (ER), progesterone (PR), and human epidermal growth factor receptor 2. However, diagnoses are commonly done in advanced stages worldwide[1]. In Mexico, some studies have reported that 6 out of 10 BC diagnoses are made between stages IIB and IV[8,9]. Identifying the clinical stage, prognostic markers, and clinical characteristics plays a key role since they may indicate the biological behavior of BC, thus determining the clinical and therapeutic treatment and survival for patients.

Nevertheless, in Mexico, the clinical characteristics of BC have been little investigated compared to the analysis of the global burden of the disease[10,11], mortality trends[12], and use of preventive and diagnostic health services[13], which is partly explained by the lack of a population-based census. Therefore, this study aimed to assess the clinical characteristics of BC among women living in the Guadalajara Metropolitan Area (GMA), which is located in the state of Jalisco, Mexico, who were treated in a tertiary care hospital during 2013-2017, as well as to analyze the distribution, differences and spatial patterns of diagnoses.

Materials and methods

The design of this study was ecological-exploratory. It was conducted at the Jalisco Institute of Cancerology (IJC per its Spanish acronym), a third-level hospital for cancer patients, located in the municipality of Guadalajara, Jalisco, Mexico, dependent on the Ministry of Health of the State of Jalisco. Ethical approval to conduct this study was obtained from the Ethics and Research Committee of the IJC (Reference PRO-12/16), as well as by the Committee of the University Center for Health Sciences of the Universidad de Guadalajara (reference CI-03920). Due to the nature of the study, which involved an analysis of secondary epidemiological data, informed consent was not required from subjects. This manuscript has been written according to the STROBE (Strengthening The Reporting of Observational Studies in Epidemiology) statement guideline. Due to the nature of the study, which involved an analysis of secondary epidemiological data, study registration was not necessary.

Data collection and inclusion criteria

According to the criteria of the Mexican Standards NOM 041-SSA2-2011[14] and the National Comprehensive Cancer Network of the United States[15], clinical records of women who were diagnosed with BC at IJC between 2013 and 2017 were used as a secondary source. Therefore, no sample or power calculation was necessary. In addition, the population of the following municipalities comprising the GMA has included: Guadalajara, San Pedro Tlaquepaque, Tonalá, Tlajomulco de Zúñiga, Zapopan, El Salto, Juanacatlán, Ixtlahuacán de los Membrillos, Acatlán de Juárez, Zapotlanejo, and Villa Corona, which is justified by territorial proximity, several interventions, and government planning[16,17]. The GMA is the second largest metropolis in Mexico, outranked only by the Metropolitan Area of the Valley of Mexico. According to the National Institute of Statistics and Geography[5], the GMA has 5,179,874 inhabitants, with four municipalities containing 69.6% of the population (Guadalajara, San Pedro Tlaquepaque, Tonalá, and Zapopan).

The subject demographics and variables collected by the clinical records were: address, age, education (categorical), employment (categorical), BI-RADS classification, genetic biomarkers, and clinical stage, the latter classified as early (stages 0, IA, IB, IIA) and late (IIB, IIIA, IIIB, IIIC, IV), according to the criteria contained in the NOM 041-SSA2-2011[14]. The exclusion criteria were women whose municipality of residence was different from those that integrated the GMA, a different diagnosis than BC, or without a clinical record to collect the variables of interest for this research.

Statistical and geospatial analysis

The sociodemographic and clinical variables were analyzed using descriptive statistics, so absolute and relative frequencies (95% confidence interval [CI]) were obtained. Furthermore, Pearson's chi-square test ($p < 0.05$) was used to compare age groups based on early or late clinical-stage classification. Data analysis was performed using IBM SPSS Statistics (version 22). Considering the residence address of the women diagnosed with BC, a geolocation process was conducted using the national geostatistical framework and Google My Maps platform, resulting in a spatial distribution map covering the diagnoses in the study area. Then, four algorithms were used in the QGIS software version 3.22.3 (Creative Commons Corporation, Mountain View, California, United States) to analyze the spatial density of the diagnoses and quantitatively identify areas with higher and lower concentrations. This analysis was conducted only in the four municipalities with the highest population density (Guadalajara, San Pedro Tlaquepaque, Tonalá, and Zapopan) to obtain precise and detailed territorial data. Thus, a vector layer was generated with a size similar to the surface of the GMA, comprised by square km grids. Subsequently, the frequency of BC diagnoses for each of these spatial units was estimated. On the other hand, the Kernel Density Estimation was used to identify the concentrated areas of diagnoses, which were compared with the population density of the GMA. In this analysis, the population parameters were carefully selected to ensure the sensitivity and reliability of the results[18]. Finally, the Kernel Density Estimation was complemented with isolines as support for delimitating the concentrated areas (concentric lines).

Results

2,385 women living in the State of Jalisco were treated at the IJC. Their BC diagnoses were made during the 5-year study period. However, only 1,245 women met the selection criteria. Table 1 shows their sociodemographic characteristics, in which the average age was 52.9 years (SD = 12.3), while the highest percentage for level of schooling was secondary school (24.6%), followed by elementary school (21.8%).

Table 1. Sociodemographic characteristics and municipality of residence of women diagnosed with breast cancer (BC) and treated at the Jalisco Institute of Cancerology (IJC), 2013-2017

Variable	n	%
Average age (years)	52.9	12.3 (SD)
Minimum age	19	
Maximum age	95	
Schooling (grade concluded)		
Elementary	272	21.8
Secondary	306	24.6
High School	172	13.8
Professional	194	15.6
No formal education	270	21.7
Unknown	31	2.5
Occupation		
Paid	212	17
Domestic work	1,006	80.8
Does not work	27	2.2
Municipality of residence		
Guadalajara	593	47.6
Zapopan	287	23.1
Tlaquepaque	125	10
Tonalá	84	6.7
Tlajomulco de Zuñiga	60	4.8
Zapotlanejo	31	2.5
El Salto	26	2.1
Ixtlahuacan de los Membrillos	10	0.8
Ixtlahuacan del Río	7	0.6
Villa Corona	7	0.6
Cuquio	5	0.4
Juanacatlan	3	0.2
Acatlan de Juarez	2	0.2
Unknown	5	0.4

Source: prepared by the authors based on clinical records provided by the Jalisco Institute of Cancerology (IJC), 2013-2017.

Table 2 shows the absolute and relative frequency for BI-RADS classification, clinical stage, and biomarkers. According to the screening mammography, most women reported BI-RADS 4 (31.3%) and 5 (24.4%), that is, suspicious and highly suggestive cases of malignancy, respectively. At the time the diagnostic was confirmed, 488 women (39.2%) were classified as early clinical stage (stages 0-IIA), while 687 women (55.2%) were diagnosed in late stages (stages IIB-IV). Concerning the biomarkers, the highest proportion was ER+

Table 2. Clinical characteristics of women diagnosed with breast cancer (BC) and treated at the Jalisco Institute of Cancerology (IJC), 2013-2017

BI-RADS	n	%
0	99	8
1	6	0.5
2	127	10.2
3	65	5.2
4	390	31.3
5	304	24.4
6	8	0.6
No data	246	19.8
Clinical stage		
0	95	7.6
IA	123	9.9
IB	16	1.3
IIA	254	20.4
IIB	195	15.7
IIIA	200	16.1
IIIB	152	12.2
IIIC	75	6
IV	65	5.2
No data	70	5.6
Biomarkers		
Estrogen receptor (ER+)	746	59.9
Progesterone receptor (PR+)	717	57.6
Human epidermal growth factor receptor 2 (HER2+)	438	35.2
Triple-Positive (ER+, PR+, HER2+)	292	23.5

Source: prepared by the authors based on clinical records provided by the Jalisco Institute of Cancerology (IJC), 2013-2017.

Table 3. Clinical diagnosis of breast cancer* (BC), according to age group of women treated at the Jalisco Institute of Cancerology (IJC), 2013-2017

Age (years)	Early diagnostic (n)	%	Late diagnostic (n)	%
15-19	1	0.1	0	0.0
20-29	11	0.9	12	1.0
30-39	38	3.2	74	6.3
40-49	161	13.7	191	16.3
50-59	148	12.6	205	17.4
60-69	95	8.1	122	10.4
70-79	27	2.3	62	5.3
80-89	6	0.5	18	1.5
≥ 90	1	0.1	3	0.3
Total	488	41.5	687	58.5

*70 cases were omitted because no histopathological study with a clinical stage report was found in the file.
Source: Prepared by the authors based on clinical records provided by the Jalisco Institute of Cancerology (IJC), 2013-2017.

(59.9%), but we also identified that 23.4% were positive for the three biomarkers considered in this study.

On the other hand, table 3 shows that, regardless of early or late diagnosis, most women were between 40-59 years old, with no statistically significant differences. Even when establishing two comparison groups, that is, women ≤ 60 years old and > 60 years old, a probability of late diagnosis of 57.3 and 61.4%, respectively, was observed. The odds ratio estimate was 1.15 (95% CI 0.65-1.09), with no statistical significance.

The distribution analysis of BC diagnoses showed that 87.5% (n = 1,089) were concentrated in the four municipalities characterized by the highest population density in the GMA: Guadalajara, Zapopan, Tlaquepaque and Tonalá (Fig. 1). Furthermore, the highest frequency of diagnoses was recorded in the northeastern area, up to 11 per spatial unit (square km), while in the southwestern area, with values ≤ 5, the contrary was observed.

The Kernel density estimation showed three areas with the highest concentration of diagnoses, which were delimited using isolines in Guadalajara northeast, Zapopan Northwest, and Tlaquepaque South (Fig. 2). On the other hand, color shading identified only one area of greater spatial density (red) in the GMA, located in Guadalajara northeast.

Discussion

The results showed a recent overview for the clinical characteristics of BC among women living in the GMA, located in the state of Jalisco, Mexico. Therefore, we identified that detecting and diagnosing BC are still being done in suspicious phases, that is, highly suggestive of malignancy or clinically advanced. Moreover, women were characterized by having a lower level of schooling, being housewives and residents of urban areas, with an average age of 53 years. On the other hand, the spatial analysis showed the concentration areas for BC diagnoses in the study area. Thus, it is appropriate to suggest that detection strategies should be implemented through breast self-examination, clinical examination, and screening mammography – secondary prevention – considering a territorial perspective,

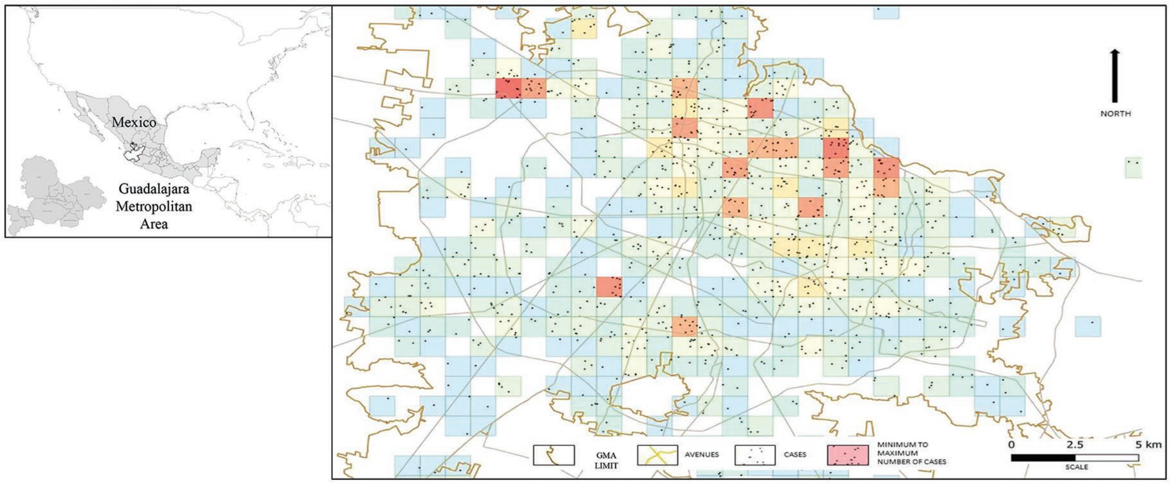

Figure 1. Distribution and frequency of breast cancer diagnoses (BC) per spatial unit (square km) in the Guadalajara Metropolitan Area (GMA), 2013-2017. *Source: prepared by the authors based on clinical records provided by the Jalisco Institute of Cancerology (IJC), 2013-2017.*

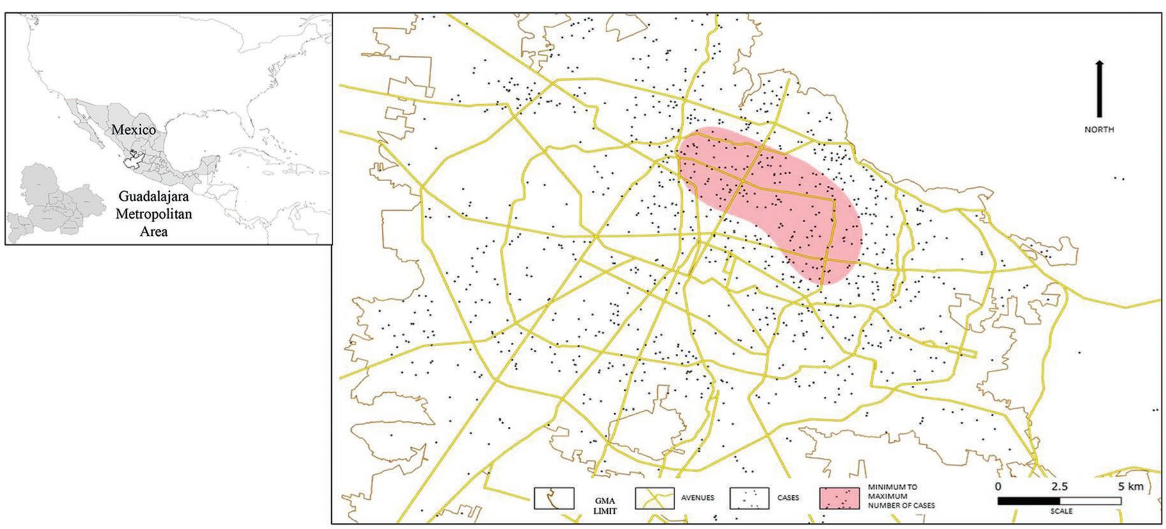

Figure 2. Spatial density for breast cancer diagnoses (BC) in the Guadalajara Metropolitan Area (GMA), 2013-2017. *Source: prepared by the authors based on clinical records provided by the Jalisco Institute of Cancerology (IJC), 2013-2017.*

that is, focusing on the places where the female population associated with risk factors for BC lives, which could certainly be complemented by the spatial analysis tools used in this study to increase the population impact of the secondary prevention strategies.

The strategy to control BC stands out for focusing on early detection of the disease to avoid the consequences attributable to late-stage BC diagnoses[19]. Therefore, BI-RADS 4, 5, or late-stage diagnoses suggest that screening programs are not effective[19]. In this sense, this situation is very likely to occur in several states of Mexico, since studies have reported late-stage BC diagnoses, particularly at 53 years of age[8,9]. Similarly, screening coverage for lower-income countries is < 23%[20], as reported by a representative study on Mexican women[13], while the Breast Cancer Program implemented by the Mexican Ministry of Health has reported a figure of 15% and a diagnostic coverage of 16%[21]. These figures may explain the detection percentages for BI-RADS 4 and 5, as well as the proportion of diagnoses in advanced stages that were identified in women living in the GMA. Primarily because in Mexico the detection process through screening mammography is characterized by being opportunistic and not preventive, attributable to failures in information systems, management, and patient monitoring, among other important aspects[21].

Since 2013, when more than 14 million women were reported in Mexico, there was a warning about the disparity between the installed capacity in clinical services for screening and the number of women aged 40-69 years[13]. The most recent population census reported approximately 19 million, which shows the potential demand for health services (prevention, detection, diagnosis, treatment, rehabilitation) and coverage for the target group. Being diagnosed with BC can be a shocking experience that, unfortunately, many women undergo worldwide[22]. Therefore, it is essential to apply secondary prevention strategies to reduce the possibility for BC to occur in advanced stages, which is associated with low survival[1] and older age. Nevertheless, our results revealed no statistically significant differences concerning early or late diagnosis between different age groups, which is in line with other studies in which age does not have an impact on the possibility for early or late diagnosis. However, this could be because of a delay in seeking professional medical care, a delay in health systems when detecting or diagnosing, or the usual place of residence – urban or rural[23,24]. Thus, a low survival prognosis (≤ 5 years) is expected when more than 3 months have elapsed since the patient identified the first symptom and the initiation of medical treatment[25]. Women who regularly practice breast self-examination are more likely to be diagnosed in the early stages, so timely detection through effective screening programs has explained the decreased mortality observed in countries such as Australia, Canada, or the United States[1].

On the other hand, since we used the Kernel Density Estimation, our results allowed us to accurately identify the distribution and concentration patterns of BC diagnoses in the GMA, as reported by other metropolitan areas of Latin America, such as Mexico City[26], or Quito, Ecuador[27]. In this sense, facing unequal access to BC care services may occur. Furthermore, there are sociodemographic elements that can explain differences and spatial patterns associated with diagnoses, for example, the distance from care services[28], degree of urbanization[29], socio-economic status and level of schooling[1,26,] or the absence of social security[28] in metropolitan cities. It is in these areas where cultural and social factors, deficiencies in health services, and economic limitations exert influence on getting appropriate diagnosis and treatment for BC. Our results suggest that neither the place of residence nor age are factors associated with early or late diagnosis, but instead, they may be related to rural residence or comorbidities, delay in seeking health care, or in scheduling health services to meet the indicators established by the NOM 041-SSA2-2011[14]. Whether the diagnosis is made in the early or late stage, the geographical distribution of BC diagnoses may show how women access to health services regarding health promotion, prevention, clinical examination, screening mammography, clinical diagnosis, treatment, and possible rehabilitation procedures.

Considering our results, the following limitations should be noted. Since data from other health institutions, municipalities of Jalisco or federal entities of Mexico were not included or analyzed, it is not possible to generalize the results, although we found similarities with other studies. Furthermore, we did not analyze socioeconomic or clinical variables that could be associated with the possibility of detecting and diagnosing BC in clinically advanced phases. Taking into account that most developing countries do not have quality information on the profile of diagnosed cancers, unless there are population-based cancer registries, which has not yet been achieved in Mexico, we note that this study collected data directly from clinical records, that is, a reliable secondary source, since it is in accordance with criteria established by the Ministry of Health regarding content and organization. Moreover, clinical management and therapeutic decisions depend mainly on the information contained in the files. Finally, we note that in the spatial analysis, specific and non-aggregate data were used, which provided a territorial perspective with greater precision in terms of the results, so spurious results were not generated.

Conclusion

This study provided recent evidence on characteristics of detection and clinical diagnosis of BC among women living in the GMA, Mexico, and showed that these processes continue to occur in suspicious phases, highly suggestive of malignancy or clinically advanced.

Furthermore, there are areas in the city where actions aimed at detecting and diagnosing the disease early could be territorially focused, that is, on a local territorial scale to increase their population impact.

Approval

Ethical approval to conduct this study was obtained from the Ethics and Research Committee of the IJC (Reference PRO-12/16), as well as by the Committee of the University Center for Health Sciences of the Universidad de Guadalajara (reference CI-03920).

Authors contribution

I.M. Ramos-Herrera, M.E. González-Castañeda, J.L. Vázquez-Castellanos, D. Mora-Plascencia, and A. Reyna-Sevilla: study conception, result interpretation and discussion. I.M. Ramos-Herrera, M.E. González-Castañeda, A. Reyna-Sevilla, J.D. Robles-Pastrana, and M.G. Carranza-Matus: study design, analysis and data interpretation. I.M. Ramos-Herrera, A. Reyna-Sevilla, S. López-Águila, R.M. Valdez-López, A. Morales-Fernández, and M. Galarde-López: manuscript preparation.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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