ORIGINAL ARTICLE

Disparities in Breast Cancer Characteristics in Mexico

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KEYWORDSBreast cancer;
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Abstract **Introduction:** There are no data on breast cancer epidemiological characteristics of patients treated in the private medicine setting in Mexico. **Methods:** A retrospective study of women treated in a private tertiary health center in Mexico City from 2001 to 2016 was carried out, and a comparison was made with data of the National Institute of Cancer (InCan). **Results:** A total of 240 patients with a median age of 52 years were included. The most common histologic subtype was ductal carcinoma, with most cases corresponding to the luminal immunophenotype. Tumors were detected by radiologic screening in 34% of cases, and in 41.7%, tumors were diagnosed in situ or at stage I, in comparison with the InCan series, where 48% are stages III and IV ($p < 0.01$). Of the cases detected by self-palpation, half had lymph node metastases vs. 7% in the screening-detected cases ($p < 0.001$). In 60%, conservative surgery was performed, and in 13%, mastectomy with immediate reconstruction. Five-year disease-free survival is higher than 90%. **Conclusions:** Breast cancer epidemiology is consistent with InCan statistics. There is significant difference in clinical stages at presentation, which is attributed to disparity in access to screening. (creativecommons.org/licenses/by-nc-nd/4.0/).

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INTRODUCTION

Breast cancer is one of the most common malignancies, with high impact on general mortality worldwide, and it represents a public health problem in Mexico. According to a recent analysis of GLOBOCAN statistics, the breast cancer-related mortality rate in Mexico has increased over the past few decades, in contrast with a decrease in the rate of mortality for this neoplasm in European countries¹. In Mexico it is the most common malignant tumor in women since 2007, when it surpassed cervical cancer. According to GLOBOCAN 2012, the national rate of incidence is 35.35 x 100,000, which is higher than the 27.2 reported in 2008². Unlike developed countries where the diagnosis is made at early stages, in developing countries, most diagnoses are made at advanced stages, with a severe negative impact on the possibility of cure³. One of the reasons for the delay in diagnosis is the consequence of difficulties in access to detection⁴. In addition to late diagnosis, other breast cancer epidemiological particularities have been reported in our country, such as presentation at earlier stages than in developed countries, which entails a higher impact on national public health services since it primarily affects women at productive age⁵. On the other hand, significant differences have been reported even within developed countries in both detection and treatment of breast cancer owing to sociodemographic and economic factors, with a direct impact on mortality^{6,7}. In developing countries, the gaps in detection and quality of care are broader than in developed countries, and Mexico is not an exception. There are no reports on epidemiological and clinical characteristics of breast cancer treated in the private medicine setting in our country. The purpose of the present work is to describe the epidemiological, clinical, and management characteristics of patients with breast cancer treated in the practice of one of the authors (HMF) in a tertiary care private hospital in Mexico City, and to compare these characteristics with those reported by tertiary care public centers in our country (National Institute of Cancer), with an emphasis on the importance of screening for early detection of this neoplasm.

MATERIAL AND METHODS

A retrospective study was carried out, which included all breast cancer-diagnosed patients (phyllodes tumors were included) treated by one of the authors (HMF) from January 1, 2001 through June 30, 2016 in a tertiary care private hospital of Mexico City. Patients treated for exclusively palliative purposes, or receiving first or second opinion care, but whose treatment was in charge of another institution or another physician, were excluded. Demographic variables, family hereditary history, and clinical and radiological characteristics were recorded, as well as histopathological and surgical variables. Descriptive statistics was used, as well as categorical variables comparison with the chi-square test and Pearson's exact test, and mean comparison with Student's *t*-test. Survival plots were constructed with the Kaplan-Meier method. All statistic calculations were performed using SPSS v20.0 software. Significance was established at a *p*-value < 0.05.

Table 1. Breast cancer patients demographic and clinical characteristics (n = 240)

Characteristic	
Age	Mean 54.73 + 14.09; Median 52 years (28-99)
Family history	26.7%
Sister	15.62%
Mother	25.0%
Daughter	6.25%
Maternal aunt	15.62%
Maternal grandmother	6.25%
Paternal grandmother	6.25%
Detection method	
Screening	34.2%
Physician	4.2%
Patient	61.7%
Laterality	
Bilateral	1.7%
Right	43.3%
Left	55.0%
Tumor size*	Mean 2.31 cm (+ 1.5 cm);
Clinical stage (AJCC) [†]	Median 1.57 (0.5-11 cm)
0	18.3%
I	35.8%
IIA	28.3%
IIB	9.2%
IIIA	1.7%
IIIB	1.7%
IIIC	1.7%
IV	2.5%

*Invasive cancers. [†]Phyllodes tumors excluded.
AJCC: American Joint Committee on Cancer.

RESULTS

A total of 240 patients were included in the study period, with a mean age of 54.73 years (+14.09) and a median of 52 years (range: 28-99). Direct family history of breast and/or ovarian cancer was found in 26.7% of patients, with the highest number of affected relatives being two sisters and one daughter in one patient in whom BRCA1 gene deleterious mutation was corroborated. Tumor distribution according to laterality was even, with a slight predominance of the left side and, in 1.7% of cases, cancer occurred bilaterally. The tumor detection method was radiological screening in 34.2%, physical examination by the doctor in 4.2%, and detected by the patient herself by palpation of a mass in 61.7%. Tumor mean size in invasive cancers was 2.31 cm, with a median of 1.57 cm (0.5-11). Clinically, 17.5% of the patients presented with lymph node involvement and 2.5% with distant metastasis. Other demographic and staging characteristics are presented in [table 1](#).

With regard to the histological type, infiltrating ductal carcinoma was predominant in 59.16% of cases, followed by ductal carcinoma in situ in 15.83%. Other histological types are shown in [table 2](#). The predominant

Table 2. Histopathologic characteristics (n = 240)

Characteristic	
Type of tumor	
Infiltrating ductal	59.16%
Ductal in situ	15.83%
<i>In situ</i> with micro-invasion	2.5%
Infiltrating lobular	10.0%
Mucinous	2.5%
Apocrine	0.8%
Tubular intracystic	0.8%
Mixed	0.8%
Benign phyllodes	3.3%
Malignant phyllodes	0.8%
Grade*	
1	10.0%
2	58.3%
3	26.7%
Molecular type†	
Luminal A	44.3%
Luminal B	35.05%
Pure HER	7.2%
Triple-negative	12.4%
Unidentified	1.0%

*Excluding phyllodes. †Only invasive cancers (n = 194).

histological grade was 2 (58.3%). Most patients with invasive cancers (n = 194) were positive for estrogen (81.4%) and progesterone receptors (75.3%), with a minority of HER2 over-expression (19.6%); in eight cases (4.2%), HER2 status is unknown. Ki-67 was determined in 176 cases (90.7%), with a median of 20 (2-90%). The predominant molecular type was luminal A (44.3%) (Table 2).

With regard to treatment, 12.5% of patients received neoadjuvant chemotherapy. Conservative surgery was performed in 60% of patients, and in 5% no resection surgery was performed due to either metastatic disease or the patient being of extremely advanced age. The type of surgery is shown in table 3. Post-surgery metastatic disease to axillary lymph nodes was reported in 43.3% of invasive cancer cases. Post-surgery histopathologic stage is shown in table 3. Postoperatively, 94.4% of patients treated with conservative surgery received adjuvant radiotherapy according to international guidelines, whereas 7.5% of mastectomy treated patients also received radiotherapy, either due to tumor size being > 5 cm, or presence of > 3 positive axillary lymph nodes. All patients with positive hormone receptors received hormone blockade, predominantly with letrozole in postmenopausal (89.9%) and tamoxifen in premenopausal and 10% of postmenopausal women. Of the group of patients with invasive cancers (n = 194), 46.4% received chemotherapy either adjuvant or as treatment for metastatic disease (2.5%), while 10.3% received trastuzumab owing to HER2 over-expression.

With a median follow-up of 36 months (range: 1-172), 14 recurrences occurred (7.2% of patients with invasive cancers), with four being local, four regional, two systemic, and four regional and systemic simultaneously. Disease-free survival was 93%, and overall survival was 96%.

An analysis of tumor characteristics was carried out in invasive cancers among those detected by screening and detected by the patient. Those detected by medical examination were included in the latter group, since they represent a very low proportion (4.2%). Smaller tumor size, absence of lymph node involvement, and lower American Joint Committee on Cancer (AJCC) clinical stage were found to be statistically significant factors in favor of the group of detection by screening (Table 4). No differences were found in age or type of surgery (mastectomy vs. conservative) according to the detection method. Another finding was a significant difference in tumor size according to histological grade, with mean tumor size in grade 2 tumors being 1.97 ± 0.97 cm vs. 3.26 ± 2.31 cm in grade 3 tumors ($p = 0.0001$).

On the other hand, a comparison of data of patients attended in a private setting was made with the breast cancer experience in the Seguro Popular era (2007-2013) using data on 3,109 cases published by Mohar A. et al. of the National Institute of Cancer (InCan) of Mexico City⁸. According to the published data, median age was 50.9 years, with no difference with 52 years in our study. In addition, more than 80% corresponded to canalicular carcinoma, without significant difference with 77.5% in our series, when infiltrating canalicular carcinoma, carcinoma *in situ*, and ductal carcinoma *in situ* with micro-invasion are combined. With regard to immunophenotype, in both series luminal is predominant, although a significant difference was documented: 79.35% in our series vs. 58.1% in the InCan series ($p < 0.05$). Similarly, pure HER subtype was less common in our series than

Table 3. Type of surgery and postoperative staging

Type of surgery	
Conservative surgery	60.0%
Mastectomy (total or modified radical)	20.0%
Skin-sparing mastectomy with immediate reconstruction	13.33%
No surgery	5.0%
Surgical biopsy	0.8%
Clearance without resection	0.8%
Post-surgical lymph node status	
N0	56.7%
N1	29.9%
N2	8.2%
N3	4.1%
Post-surgical histopathologic stage (AJCC)*	
0	14.2%
I	27.5%
IIA	25.0%
IIB	16.7%
IIIA	5.0%
IIIB	2.5%
IIIC	3.3%
IV	2.5%

*Phyllodes tumors are excluded.
AJCC: American Joint Committee on Cancer.

Table 4. Demographic and histopathologic characteristics according to detection method

Age	Screening	53.24 + 11.32 years	p = 0.07
	Patient/physician	55.51 + 15.34 years	
Tumor size	Screening	1.19 + 0.40 cm	p = 0.0001
	Patient/physician	2.80 + 1.63 cm	
Positive lymph nodes	Screening	7.3%	p = 0.0001
	Patient/physician	48.71%	
Conservative surgery	Screening	75.6%	p = 0.105
	Patient/physician	60.56%	
Stage	Screening	Patient/Physician	
	(34.1%)	(65.9%)	
0	38.5%	1.3%	
I	46.2%	19.0%	
II	10.2%	58.0%	
III	2.5%	15.2%	
IV	0	3.8%	p = 0.0001

in the InCan series (7.2 vs. 21.9%; $p < 0.05$), with the same being observed for triple-negative status (12.4 vs. 17.2%), although in this case the difference was not statistically significant. The main difference between both series lies in tumor stage at presentation. Although the InCan series does not specify the method for tumor detection (screening vs. patient or doctor detection), stages at presentation are significantly more advanced than in our series. In this way, stage zero or carcinomas *in situ* accounted only for 1.9% of cases in the InCan series vs. 14.2% in our series ($p < 0.05$); no significant differences were found for stage I, with 21.6 vs. 27.5% in the InCan and the present series, respectively, but in stage II, cases were more common in our series (41.7 vs. 29.2% in the InCan series), and stages III and IV were significantly less frequent in our series (10.8 vs. 34.5% and 3.8 vs. 13.5%, respectively; $p < 0.05$).

DISCUSSION

Breast cancer is the leading malignant neoplasm in women in Mexico, and as in other countries of Latin America, it often appears at advanced stages with high associated mortality⁹. There are very limited data on epidemiological, clinical, histopathological, and surgical characteristics of breast cancer managed in private medicine settings where, by definition, greater access to both screening and best available treatments is generally possible. Most series in our country come from large public health institutions, such as the National Institute of Cancer. In the present series we found that patient age does not differ from that of women attended to in public institutions, and this is corroborated with observations already published in other series that have established that, on average, breast cancer onset in our country occurs up to one decade earlier than in the USA or Europe^{5,10}. The infiltrating canalicular histologic type is not different from that reported by national and international series; however, the immunophenotype was significantly different, in particular with a lower proportion of the most aggressive

subtypes, namely, pure HER2 and triple-negative, although in the latter the difference was not statistically significant with regard to the InCan series (12 vs. 17%). However, in another series of the same institution of 2,074 Hispanic women treated from 1998 to 2008, the prevalence of triple-negative breast cancer was 23.1%, mainly associated with young age, premenopausal status, high histological grade, and more advanced disease¹¹. The lower frequency of aggressive cancers in our series is also reflected in the lower frequency of high-grade tumors in our series compared with the InCan series (26.7 vs. 46.8%).

The main difference between our series and the InCan series and other national and Latin American public hospitals is the stage of the disease at presentation. In one study conducted among 138 Mexican oncologists, 58% of new breast cancer cases were reported to be diagnosed at stages III and IV¹² (48% in the InCan series and 13.3% in ours). One possible explanation for the difference in stages at presentation is not only the disparity in health services availability, specifically open population screening, but, at least in part, since this was a surgical series, there is reference bias with a tendency to occur with the surgeon at earlier stages than with the medical oncologist or a national health institution.

Another significant difference is that in the InCan referred study¹², 63% of patients underwent mastectomy, in comparison with 60% of conservative surgery in our series, whereas 13.3% of patients, although undergoing mastectomy, were immediately reconstructed. The main reason for presentation at advanced stages is the limited access to screening by the general population, which is in clear contrast with the population attended to in private medicine settings, where 34% of cases are detected by this method. However, there is still a majority that, even with access to health services, is still detected by the patient, generally at advanced stages. The main effect of screening is a reduction in the frequency of advanced cancer cases. In a Swedish study, a reduction of more than 20% in advanced cancers translated into a 28% reduction in breast cancer-related

mortality in women invited to screening¹³. In our series, it is clear that in screening-detected women, 84.7% had early stages (stages 0 and I), whereas in 77% of women whose neoplasm was detected by self-palpation or physical examination by the physician, it was at advanced stages (stages II, III, IV). The proposed mechanisms by means of which screening reduces breast cancer-related mortality are the detection of smaller tumors, negative lymph nodes, and lower tumor grade¹⁴. In our series, when the comparison of screening-diagnosed patients vs. patients whose neoplasm was detected by self-palpation was made, significant differences were found in tumor size (mean 1.19 vs. 2.80 cm; $p = 0.0001$), positive axillary lymph nodes (7.3 vs. 48.7%; $p = 0.0001$) and tumor size according to the grade: mean tumor size in grade 2 tumors was 1.97 ± 0.97 cm vs. 3.26 ± 2.31 cm in grade 3 tumors ($p = 0.0001$). Evidently, detection by self-palpation is not useful for early stage diagnosis, since when this occurs, the tumor measures an average of 2.8 cm and nearly half of patients will have metastasis to axillary lymph nodes.

The main strength of this series is that it represents the practice of a single surgeon (HMF) in the same institution, without variability in both diagnosis and treatment criteria. The differences in stages at diagnosis are essentially due to disparities in health services availability, a highly prevalent situation in Latin America and other developing countries, but also already reported in the USA^{15,16}, Europe^{6,17} and other countries of the world. In fact, an analysis of GLOBOCAN statistics has been conducted, demonstrating that breast cancer-related mortality is directly associated with the Human Development Index¹⁸, with one of the reasons being late detection, aggravated by unavailability of best treatments. The main weakness of the present series is the sample size, which may not be representative of nation-wide private practice, which warrants the performance of prospective studies with a representative sample of this population.

In conclusion, in a sample of patients treated in a tertiary care hospital with access to all diagnostic and therapeutic resources, breast cancer onset occurs at the same age as at the national level, with a lower proportion of aggressive phenotype tumors and, especially, with diagnosis at earlier stages of the disease, with the breast being able to be preserved in a significant proportion of patients, and with an excellent long-term survival. Inequity of health service access is a situation that must be resolved in government organizations.

DECLARATION OF INTEREST

The authors declare not having any conflicts of interests.

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