

Prevalence of Known Risk Factors in Uruguayan Women Treated for Breast Cancer at a University Hospital

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ABSTRACT

INTRODUCTION: In Uruguay, breast cancer has the highest incidence and mortality of all cancer in women. Knowledge of the distribution of risk factors related to disease development supports the implementation of prevention strategies in routine clinical practice. This study aimed to determine the epidemiological profile for breast cancer and the frequency of mammographic surveillance in the surveyed population.

MATERIALS AND METHODS: A survey was conducted among Uruguayan women diagnosed with breast cancer who were assisted in the mastology unit of the oncology service of the Hospital de Clínicas in Montevideo, Uruguay, from September 1, 2018, to March 1, 2020.

RESULTS: This study included 398 respondents, with a median (SD) age at diagnosis of 61 (34–86) years. A total of 310 respondents (78.0%) had 1 or more risk factors. Most women aged over 50 years (264 out of a total of 338 [78.1%]) underwent mammographic surveillance at least biennially.

CONCLUSIONS: Consistent with international reports, most respondents had a risk factor. Among the group of respondents aged over 50 years, most underwent mammographic and clinical surveillance at least biennially. Although it is only possible to formulate conclusions about the surveyed women because of the study design, the obtained data further our understanding of the epidemiological profile of the Uruguayan population, which can contribute to prevention practices.

KEYWORDS: Breast cancer risk factors, breast cancer prevention, body mass index, mammography, breast cancer screening

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Introduction

Cancer is an important epidemiological issue in Uruguay. Considering both sexes, cancer is the second cause of death, after cardiovascular diseases, and accounts for almost a quarter (24.6%) of all deaths registered in the country per year. More than 16 000 new cases are registered per year, and approximately 8000 Uruguayans die of the disease.^{1,2}

As observed worldwide, breast cancer is the most frequent cancer diagnosed among women in Uruguay and the main cause of cancer-related deaths. Each year, approximately 1900 new cases are registered and approximately 670 women die from this disease. In Uruguay, 1 in 11 women will develop breast cancer over the course of a lifetime. The median age of patients diagnosed with their first invasive breast cancer from 2012 to 2016 was 63 years (51–74 years). Most patients (69.5%) are diagnosed at an early stage, which reinforces the importance of secondary prevention for this pathology.^{3,4}

There has been a decrease in the mortality rate of this disease in recent years, which could be associated with an increase

in early detection, improved treatments, and integration of interdisciplinary teams for this pathology,² but breast cancer continues to represent a great burden both socially and economically. The economic burden of breast cancer for society is defined by direct costs related to medical care and indirect costs including disability, absenteeism from work, and widows' and orphans' pensions. Hence, it is important to develop policies and programs for the prevention and control of this disease.

The primary prevention of breast cancer is focused on adjusting risk factors that are subject to change and promoting protective factors. As with most cancers, the etiology of breast cancer is unknown, but several risk factors have been implicated. These can be classified as modifiable and nonmodifiable (Box 1). Determining the distribution of risk factors is essential for implementing interventions in the community to promote the well-being and health of women.

The clinical practice guidelines for early detection of breast cancer of the Ministry of Public Health (Ministerio de Salud Pública [MSP]) have recommended systematic mammography



Box 1. Protective factors and modifiable and nonmodifiable risk factors for developing breast cancer.

Nonmodifiable risk factors

- Female gender
- Increasing age
- Earlier menarche or later menopause
- Nulliparity or increasing age at first pregnancy
- Dense breast tissue
- Personal history of in situ or invasive breast cancer or proliferative lesions
- Family history of breast cancer
- Inherited genetic mutations

Modifiable risk factors

- Overweight and obesity
- Alcohol
- Menopausal hormone therapy

Protective factors

- Breastfeeding
- Physical activity

screening every 2 years for women aged 50 to 69 years, an age range in which the benefit of mammography screening is greater and the risks are lower (overdiagnosis, false positives). The potential benefits and risks of conducting this study should be individualized and analyzed in women aged 40 to 49 years and 70 years or older.

Although there is no evidence to support the effectiveness of clinical breast examination screening for breast cancer, considering the cultural characteristics of our population our guidelines recommend the inclusion of an annual clinical breast examination as a way to stimulate clinical controls.

This study aimed to determine the epidemiological profile of breast cancer and the frequency of clinical and mammographic surveillance of patients diagnosed and treated for breast cancer in the Mastology Teaching Unit (Unidad Docente Asistencial de Mastología [UDAM]) of the Oncology Service of the Hospital de Clínicas.

Materials and Methods

This observational and prospective study included patients aged 18 years or older who were diagnosed with breast cancer and were assisted at the UDAM of the Oncology Service of the Hospital de Clínicas from September 1, 2018, to March 1, 2020.

Hospital de Clínicas is a public hospital in the capital city of Montevideo, in Uruguay. It belongs to the Faculty of Medicine of the University of the Republic and is a reference institution. As it is a general hospital, the patients who were included in this study were referred from gynecology, surgery, and general medicine services as well from other public hospital from other cities in the country.

All patients signed an informed consent form and authorized the use of the information in this study.

This survey was designed ad hoc to comprehensively investigate the main risk factors for developing breast cancer, the

patients' level of education, and the completion of clinical breast examination and mammography screening. It comprised 15 closed, dichotomous, or multiple-choice questions. These were designed to determine the prevalence of the main risk factors for breast cancer and the participant's level of education, smoking habits, and frequency with which clinical breast examinations and mammography screenings were performed.

The included variables were age at diagnosis, anthropometric measurements (height and weight at puberty, at diagnosis, and at present), family history of breast cancer, personal history of proliferative breast diseases, high breast density, hormonal factors, alcohol consumption, and physical exercise.

The anthropometric data were based on the patients' reports on weight at diagnosis, at present, and at puberty; whether the weight variation between puberty and diagnosis was greater than 10% was also considered. The weight and height data were used to determine the body mass index (BMI), and the World Health Organization classification was used, which considers normal BMI as 20 to 24.99 kg/m², overweight as 25 to 29.9 kg/m², and obese as 30 kg/m² or more.⁵ Since there were no previous values, the sample size was calculated to estimate a ratio assuming an inaccuracy of 0.05 and an expected ratio of 0.5, which resulted in the requirement of including 384 patients.

The data were collected, analyzed, and compared with the available Uruguayan data. The proposed study was conducted in accordance with the international ethical standards for biomedical research, Mercosur rules for clinical trial regulations, and the Declaration of Helsinki and with the research regulations approved by the National Ethics Committee in 2019.

Results

The study included 398 respondents, 402 patients were assisted at the UDAM of the Oncology Service of the Hospital de Clínicas from September 1, 2018, to March 1, 2020, and 398 signed the informed consent form and authorized the use of the information in this study.

The median (SD) age of the respondents at diagnosis was 61 (34-86) years. At the time of diagnosis, 114 patients (28.6%; 95% confidence interval [CI], 24.1%-33.0%) were aged 50 to 59 years, and 224 patients (56.3%; 95% CI, 51.4%-61.2%) were aged 60 years or older. Most respondents (356 [89.4%]; 95% CI, 86.4%-92.4%) were postmenopausal. The rest of the data are shown in the Table 1.

Regarding the level of education, 116 patients (29.1%; 95% CI, 24.6%-33.5%) had completed primary education, 102 (25.6%; 95% CI, 21.3%-29.9%) had started secondary education, and 24 (6.0%; 95% CI, 3.7%-8.3%) had attended tertiary education. The rest of the data are shown in the Table 1.

A total of 310 respondents (77.9%; 95% CI, 73.8%-82.0%) had 1 or more risk factors for breast cancer. Of these, 175 (45.0%; 95% CI, 40.1%-49.9%) had only 1 risk factor, 75 (18.8%; 95% CI, 15.0%-22.6%) had 2 risk factors, and only 56 (14.2%; 95% CI, 10.7%-17.5%) had 3 or more risk factors. The distribution of the risk factors is shown in the Box 1.

Table 1. Sociodemographic characteristics of patients (N=398).

VARIABLE	N (%)	95% CI
Age at diagnosis, y ^a		
≤35	4 (1.0)	0.02-1.98
36-49	56 (14.1)	10.7-17.5
50-59	114 (28.6)	24.2-33.0
>60	224 (56.3)	51.4-61.2
Menopausal status at diagnosis		
Premenopausal	42 (10.6)	7.6-13.6
Postmenopausal	356 (89.4)	86.4-92.4
Level of education		
Not completed primary education	78 (19.6)	15.7-23.5
Completed primary education	116 (29.1)	24.6-33.5
Not completed secondary education	102 (25.6)	21.3-29.9
Completed secondary education	78 (19.6)	15.7-23.5
Tertiary education	24 (6.0)	3.7-8.3

Abbreviation: CI, confidence interval.

^aMedian age at diagnosis was 60 y.

A total of 360 (93.0%; 95% CI, 90.5%-95.5%) respondents had children: 312 (84.3%; 95% CI, 80.6%-88.0%) had children before they reached the age of 30 years, and most (254 patients [63.8%]; 95% CI, 59.0%-68.5%) had breastfed an infant for more than 6 months.

A total of 136 respondents (34.7%; 95% CI, 29.5%-38.9%) had a family history of breast cancer: 90 (22.6%; 95% CI, 18.5%-26.7%) had at least 1 affected first-degree relative, 60 (15.0%; 95% CI, 11.6%-18.6%) had at least 1 affected second-degree relative, 45 (10.0%; 95% CI, 7.1%-13.0%) had 2 or more affected relatives, and 34 (8.5%; 95% CI, 5.8%-11.2%) had 2 or more affected relatives, with 1 of those being a first-degree relative. Of the 136 respondents with a family history of breast cancer, 24 had a family member diagnosed with breast cancer before the age of 50 years, and 12 had a family member diagnosed before the age of 45 years.

Among the postmenopausal respondents, 320 (80.4%; 95% CI, 76.5%-84.3%) went through menopause at the age of 45 to 55 years, 18 (4.5%; 95% CI, 2.5%-6.5%) had a late menopause (after the age of 55 years), and 59 (14.8%; 95% CI, 11.3%-18.3%) had an early menopause (before the age of 45 years). Most respondents (374 [94.0%]; 95% CI, 91.7%-96.3%) did not receive hormone replacement therapy (HRT). Of the 20 respondents who received HRT, 12 received combined HRT for 3 years, 6 received progestogens for 3 years, and no data were available for 2 respondents.

Regarding the risk factors related to lifestyle, the mean BMI at the time of diagnosis was 28.2 kg/m². Moreover, 126 patients

(31.7%; 95% CI, 27.1%-36.3%) were overweight (BMI, 25-29.9), 132 (33.2%; 95% CI, 28.6%-37.8%) were obese (BMI ≥ 30), and 140 (35.2%; 95% CI, 30.5%-39.9%) had a normal weight (BMI ≤ 25). Most patients (286 [71.9%]; 95% CI, 67.5%-76.3%) had a weight gain of more than 10% since puberty at the time of diagnosis.

A total of 306 respondents (76.9%; 95% CI, 72.8%-81.0%) exercised regularly: most (234 [58.8%]; 95% CI, 54.0%-63.6%) walked for at least 30 minutes thrice a week, and the other respondents performed other types of exercise (28, bicycle riding; 14, yoga; 4, tai chi; 8, exercise using several machines; 6, gymnastics; 4, swimming; and 4, Pilates exercise). The rest of the respondents (23.1%; 95% CI, 19.0%-27.2%) were sedentary.

More than half of the respondents (296 [74.4%]; 95% CI, 70.1%-78.7%) did not consume alcohol. Of the total of alcohol consumers, 56 (54.9%; 95% CI, 45.2%-64.6%) consumed fewer than 3 drinks per week.

Regarding smoking, most respondents (258 [64.8%]; 95% CI, 60.1%-69.5%) did not smoke, 96 (24.1%; 95% CI, 20.0%-28.3%) were former smokers, and 44 (11%; 95% CI, 8.0%-14.2%) were smokers.

Of the 338 patients older than 50 years at diagnosis, 264 (78.4%; 95% CI, 74.0%-82.8%) underwent mammographic and clinical surveillance at least biennially; the rest did not undergo mammographic surveillance or clinical breast examination on a regular basis. Of the 264 postmenopausal respondents undergoing surveillance mammography, 88 (33.3%, 95% CI, 27.6%-38.9%) had high-density breasts and went for a routine breast ultrasound (as is our usual practice for high density), and 24 of these women (9.1%, 95% CI 5.6-12.5%) underwent a breast biopsy.

Discussion

The etiology of breast cancer is unknown, although several studies have investigated the risk factors that can predict and quantify the risk of developing the disease. However, breast cancer is sporadic most of the time, and it is not possible to identify risk factors other than sex and age.

Breast cancer was diagnosed after the age of 50 years in 84.9% of the patients, with a median age at diagnosis of 61 years, which is consistent with national⁴ and international⁶ reports. Of the 398 respondents, 310 (78.0%) had 1 or more risk factors for breast cancer, which is higher than the frequency of 43.0% reported by the National Breast Cancer Program (Programa Nacional de Cáncer de Mama)⁷ and of 48.0% according to our team.⁸ This can be explained by the fact that these studies included healthy patients, whereas our study included patients with breast cancer. Moreover, our results are similar to those reported in a study by Hines et al⁹ that found that 62.0% to 75.0% of non-Hispanic patients diagnosed with breast cancer had at least 1 risk factor for the development of the disease.

Of all respondents, 136 (34.7%) had a family history of breast cancer, and 90 (22.6%) had an affected first-degree

relative. This value is higher than that of international reports, with values ranging from 15.0% to 25.0%.^{9,10} However, only 24 respondents had a family member diagnosed with breast cancer before the age of 50 years and 12 before the age of 45 years. These results suggest that family history could play an important role in the development of breast cancer in our population, although a control group would be required to confirm it. This might be due, at least in part, to the association between family history and breast cancer; however, the risk of breast cancer may be attributable not only to hereditary genetic factors but also to other factors such as shared environmental and lifestyle factors or a combination of both.

Patients with a significant family history of breast cancer or breast cancer diagnosed before 45 years old were referred to our Oncogenetics Unit for counseling and possible testing of germline BRCA1 and BRCA2 mutations. The identification of carriers of breast cancer susceptibility genes in patients and family members is an important component of the prevention strategies. When carriers are identified this should lead, after appropriate discussion, to frequent breast imaging surveillance for the early detection and treatment of cancer or risk reduction surgeries (mastectomy or salpingo-oophorectomy).

Regarding protective factors, most respondents (306, 76.6%) practiced physical exercise, and only 23.4% were sedentary. Although the populations are different, this result is similar to that found in the First National Survey for Risk Factors for Chronic Non-Communicable Diseases (CNCD), in which 22.8% of women aged 25 to 64 years and 28.0% of women aged 55 to 64 years were sedentary.¹¹ However, the social desirability bias may be an issue when interpreting our data regarding to physical exercise, which means a tendency of respondents to answer questions in a manner that will be viewed favorably by others. This bias could have been present in our results and this would be taken in consideration for future surveys with questions to encourage the respondents to answer more honestly by neutral questions (for example, do you exercise?)

Although childbirth before the age of 30 years and lactation are considered protective factors in the genesis of breast cancer, most respondents had children before the age of 30 years (312; 86.6% of this subgroup), and most (254 patients; 70.5%) had breastfed an infant for more than 6 months.

A total of 102 (25.7%) respondents consumed alcohol, which is lower than the 37.4% reported in the first CNCD, and most of those who consumed alcohol (56; 54.9%) did so fewer than 3 times a week. Although it is difficult to analyze the association between smoking and the development of breast cancer, because up to 50% of female smokers consume alcohol, several studies suggest that there is a higher risk of developing breast cancer in the smoking population,¹² and this was, therefore, included in the investigated risk factors. Only 44 respondents (11.1%) were smokers, which is lower than the 25.4% reported in the second CNCD. However, it should be noted that 96 respondents (24.1%) were former smokers, which could reflect the impact of the implementation of an important set of actions

by the state, adapting the measures proposed by the framework convention on tobacco control.

Various studies have indicated that the increase in both weight and BMI from adolescence to the age close to diagnosis is associated with an increase in the relative risk of developing this disease in post-menopause.¹³

Most of the patients (286, 71.9%; 95% CI, 67.5-76.3) had a weight gain greater than 10% since adolescence to time of diagnosis. It is appropriate to observe that the data obtained regarding weight in adolescence and at the time of diagnosis in our study has limitations in terms of their accuracy, since they are conditioned by respondent's memory. To reduce bias, the patients were also asked about their perception of weight change, specifically if it was above 10% in that period of time (adolescence-diagnosis). However, main risk factor related to weight is a higher BMI and/or the perimenopausal weight gain that have been consistently associated with breast cancer among postmenopausal women.¹⁴ In our study, 126 respondents (31.7%) were classified as overweight (BMI, 25-29.9) and 132 (33.2%) as obese (BMI \geq 30). These results are similar to those reported by the second CNCD, with values of 32.7% and 29.2%, respectively.¹¹ Because overweight and obesity were the most frequent risk factors and considering that overweight, obesity, and nutrition-related diseases (cardiovascular, metabolic, mental health, and osteoarticular diseases) are the causes of the main risk factors that affect morbidity and mortality in Uruguay, the education of postmenopausal patients would be of great importance, both to those with a diagnosis of breast cancer and to those without, to maintain a normal body weight as a preventive measure.

Our results show that some of the risk factors found in Uruguay are similar to those found in developed countries, which is most likely associated with factors inherent to the Western lifestyle. In particular, this involves demographic factors (the risk of experiencing cancer in general, and breast cancer in particular, is associated with age) as well as overweight and obesity.

Regarding education, the level of education could be related to the accessibility to patients of available information on the early detection and timely treatment of breast cancer. In this context, most of the included patients (320 [80.4%]) had completed primary education and at least started secondary education, and most of the respondents aged 50 years or older underwent mammographic and clinical surveillance at least biennially (264 patients [78.1% of this subgroup]). Such a relatively high percentage probably reflects not only the level of education but also that of the prevention campaigns performed by the Honorary Commission for the Fight Against Cancer (Comisión Honoraria de Lucha Contra el Cáncer [CHLC]) and the MSP. Therefore, the continuation of early detection programs for breast cancer should be considered a priority. This also might explain why most patients were diagnosed with breast cancer following screening mammography (258 patients [76.3%]) or medical examination (56 patients [16.5%]), whereas only 24 patients (6.0%) were diagnosed following breast self-examination.

This is consistent with previously reported data that 70% of the breast cancers assisted at the UDAM were diagnosed with stage 0 to stage II.

Among the strengths of this study, the number of included patients, the incorporation of all age groups, and the assessment of modifiable and nonmodifiable risk factors are worth noting. However, when interpreting the obtained results, it should be kept in mind that the survey was performed on patients assisted at the UDAM of the Oncology Service of the Hospital de Clínicas, which could have introduced biases and, consequently, limits the possibility of extrapolating the results to the general population. Therefore, further studies on risk and protective factors for breast cancer in a larger population, including patients assisted in private institutions and from the interior of the country, are required.

Conclusions

Although it is only possible to formulate conclusions about the women included in the survey owing to the characteristics of the study, the collected data allow us to better understand the epidemiological profile of the Uruguayan population, which can contribute to prevention practices. According to international reports, most respondents had a risk factor other than sex to develop the disease. The percentage of respondents with a family history was higher than that found internationally. Most respondents older than 50 years underwent mammographic and clinical surveillance at least biennially. This undoubtedly reflects the impact of the prevention campaigns performed by the CHLC and MSP.

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Author Contributions

CC, NC, LD contributed to the conception and design of the work; All authors were responsible for the acquisition the data.

CC, NC and RA did the analysis of data and the draft of the article; LD critically revised the article; and all authors approved the final version of the article.

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