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Breast Cancer Thirty Years Later: A Comparative Study between A 1983-1984 AND A 2012-2013 Cohorts of Argentine Women

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Abstract

Background: In Argentina the breast cancer is the most common cancer among women with an incidence rate (ARS) of 71, 2 x 100,000. Changes in the patterns of behavior of women in the last 30 years with the adoption or increase of certain behaviors considered as risk factors for breast cancer may influence on the clinical, surgical, pathological and epidemiological patterns of presentation of the breast cancer.

Purpose: A comparative study of the characteristics of the breast cancer in two cohorts of Argentinean females with a difference of 30 years at the time of diagnosis (1983-2013) was made to show differences, if any, between the profiles of presentation and diagnosis.

Methods: Data available in both series were age at recruitment, menstrual history (menarche, menopause), exogenous hormone use and reproductive history. Medical data: breast self-examination (knowledge and practice), personal breast pathology history, personal and family history of breast cancer were available in both series. TNM clinical staging, histological diagnosis and diagnostic methodology data (self-breast examination, clinical examination and mammography) were also available. Variables evaluated in both studies were compared settling down the statistical significance of the differences observed.

Results: The first series (1983-1984) was constituted by 1658 cases and the second (2012-2013) by 1732 cases.Both series are mostly made up of menopausal women (73, 9% vs. 72, 3 %) with a same average age of 59 at the time of diagnosis. Similar menstrual history (menarche: 44, 0% vs. 38, 6%). Cultural behaviors show: increased use of oral contraceptives (13, 4% vs. 37, 2 %), same number ofnulliparous (23, 1% vs. 19, 9 %),primiparous over 30 years of age declined (21, 2% vs. 11,7%) and breastfeeding more practiced (66, 0% vs.95, 0%). In the family history of BC an increase (20, 9% vs. 27,9%) was observed. Staging of tumors showed similar *"early stages"* (0-IIIa) (88, 6% vs. 87,9%)and histology more *"in situ"* forms (2,5% vs.12,0%) in the most recent series. The practice of mammography high in both series showed a significant increase (82, 4% vs.94, 1%)

Conclusion: Taken together the two cohorts show an epidemiological and clinic profile of "western" populations with few differences in presentation's profile in 30 years. If one considers our population cultural and genetic background with a strong European component the expected change in the presentation's profile of the female breast cancer seems to need more than one generation to occur and to resemble that of the geographic region in which we are located (South America) and the levels of "Less developed regions" and "Medium human development "we have achieve as a country.

Keywords: Breast cancer, Female, Argentina, Epidemiological profile.

Introduction

As in many developing countries in Argentina the breast cancer (BC) is the most common cancer among women with an incidence rate (ARS) of 71, 2 x 100,000 according to Globocan2012 [1]. Incidence rates of breast cancer have increased in most countries and regions of the world in the past few decades [2-4]. Breast cancer incidence and mortality have been increasing steadily in South-America region and in Argentina throughout the past 25–30 years [5]. Argentina, together with Uruguay (incidence rate (ARS) of 69.8 x 100,000), constitutes a cluster of women with high incidence rates for BC, not only in the world (incidence rate (ARS) of 43.1 x 100,000), but also in all Latin America (incidence rate (ARS) of 47, 2 x 100,000) and South America (incidence rate (ARS) of 52.1 x 100,000) [1].

The unavoidable changes in the patterns of behavior of women in the last 30 years [6] with the adoption or increase of certain behaviors considered as risk factors for BC cancer may influence

on the clinical, surgical, pathological and epidemiological patterns of presentation of the BC.

As a hypothesis we consider that the study of the characteristics of presentation and diagnosis of BC in two populations from the same geography but separated from each other in time by 30 years with the consequent cultural and demographic changes, implementation of preventive programs to inform women of the benefits of adopting healthy habits, early diagnosis and with better medical coverage [7-9] will allow us to show differences, if any, between the profiles of presentation and diagnosis of BC in the past and in the present.

If these differences exist, they should show a "profile of presentation" of the BC with at least a tendency to resemble that one observed in the countries of the geographical region to which we belong (South America) and the level of "human development" (Medium) achieved as a society (2,5,7).

For this purpose we reanalyzed the data available from two series of BC in our country and studied by us, one from 1983-84 [10] and the other from 2012-13 [11].

Materialsand Methods

Data collection

The data of two series of histologically confirmed BC were analyzed and compared. The first series was composed of cases diagnosed during the years 1983 and 1984. The second one consisted of cases diagnosed during the years 2012 and 2013. Both series were composed by cases reported by physicians, dedicated to the diagnosis and treatment of BC, to "collaborative groups" created for that purpose; both series were organized and analyzed by the Epidemiology Research Institute (National Academy of Medicine of Buenos Aires).

Variables studied

Data available in both series were age at recruitment, menstrual history (age at menarche, menopause), oral contraceptive (OC), reproductive history [full-term pregnancy, number of full-term pregnancies, age at first full-term pregnancy, breastfeeding practice]. In addition, it was available the following medical data: breast self-examination (knowledge and practice), personal breast pathology history, personal and family history of breast cancer. TNM clinical staging and histological diagnosis were also collected. Diagnostic methodology data (self-breast examination, clinical examination and mammography) were also available.

Statistical analysis

Data were analyzed using tests of independence Chi-Square, followed by Z tests to compare proportions. When the conditions for the conduct of these tests were not met, Fisher's exact test was used. For Chi-square test the value of the statistic, degrees of freedom (df) and the associated probability value is reported. For the Z test the P value was reported. In all tests, a significance level of 5% was set. The Chi-square and Z test were implemented in Excel spreadsheet. Fisher's exact test was performed on the R [12].

Results

Data collection

The first "collaborative group" (1983-1984) was constituted by 86 physicians, from both public (65) and private (21) health services, which reported 1658 cases. In the second "collaborative group" (2012-2013) 72 physicians, from both public (26) and private (49) health services, reported 1732 cases. Both series were analyzed by the same researchers who carried out the present study within the institutional framework of the Epidemiological Research Institute (National Academy of Medicine of Buenos Aires).

Age at diagnosis

The ages of onset (Table 1) show, in both series, a predominance of cases in the 55-64 age group. The median age was of 59, 05 and 59 years for the 1982-1983 and the 2012-2013 series respectively. There is a similarity in distribution by age group up to 75 years. Above this age, one an (statistically significant) increased frequency of cases in the 2012-13 series (9.9% vs. 15.9%)was observed.

Gynecological history

Menarche : The distribution by age of onset of menstruation (Table1) shows no difference in the different groups, from under 12 to over 17 .The age group 13 to 14 years proved to be the most frequent in both series with very similar percentages (44.3 vs. 40.6).

Menopause: In both series, about 72% of patients were postmenopausal at time of diagnosis (Table 1). The median age of onset of menopause was 50 years for the 1982-1983 series and 49 years for the 2012-2013 series.

Reproductive history

Parity: There are no significant differences regarding the number of nulliparous present in each series (23, 1% vs. 19, 9 %) (Table 1).

Children ever born: While there is, nearly, no difference in the 2 children group (39,1% vs 35 %)there are two differences: in the only 1 child group there is a statistically significant decrease in the 2012-13 series while in the 3 or more children group there is a statistically significant increase (Table 1).

Age ≥30 years at first full-term pregnancy: There is a statistically significant decrease of nearly half of cases in the 2012-13 series (21, 2% vs. 11, 7%) (Table 1).

Oral contraceptive: Data show a statistically significant increase of 2.8 times of cases (13, 4% vs. 37, 2 %) in the 2012-13 series in the use of this type of contraceptive (Table 1).

Breastfeeding: A one and a half, statistically significant, increase in their practice (66, 0% vs.95, 0%) it is shown in the 2012-2013 series (Table 1).

Personal history of breast pathology: It is observed, in the 2012-13 series, an increase of 8.1 times only in the history of dysplasia (1, 6% vs. 13, 1%); no significant difference between each series was observed in history of Atypical hyperplasia /CIS /Atypical lobular hyperplasia and Breast Cancer (Table 1)**.**

Family history of breast cancer: A statistically significant increase is seen in the 2012-2013 series (20, 9 % vs. 27, 9) (Table 1).

Bilaterality: A higher percentage of bilateral cases in the 2012-2013 series (1, 69 % vs. 3, 06%)without statistical significance is observed (Table 2).

TNM Clinical stages: Although not strictly comparable due the

Table 1: Breast cancer. Clinical characteristics. Comparative between 1983-84/2012-2013 series

Variables	1983-84 (n: 1658)	2012-13 (n: 1732)	p
Age at diagnosis (years), n (%)			
Less 40	136 (8.2)	147 (8.5)	0,765
40-44	157 (9.5)	147 (8.5)	0,317
45-49	183 (11,0)	176 (10.2)	0,407
50-54	212 (12.8)	213 (12.3)	0,668
55-64	463 (27.9)	422 (24.3)	0,018
65-74	343 (20.7)	338 (19.5)	0,394
75 more	164 (9.9)	275 (15.9)	< 0,001
Unknown	---	14 (0,8)	
Menarche by age- groups, n (%)			
12 and less	731 (44,0)	668 (38,6)	0,036
13- 14	734 (44,3)	703 (40,6)	0,334
15 - 16	170 (10,4)	168 (9,7)	0,946
17 and more	16 (0,9)	17 (1,0)	0,850
Unknown	7 (0,4)	176 (10,1)	
Menopause (presence), n (%)			
Yes	1226 (73,9)	1252 (72,3)	0,276
No	432 (26,1)	396 (22,9)	0,031
Unknown	---	84 (4,8)	
Parity, n (%)			
Nulliparous	383 (23,1)	345 (19,9)	0,024
With children	1275 (76,9)	1387 (80,1)	0,024
Childreneverborn, n (%)			
1	313 (24,5)	239 (17,2)	<0,001
2	499 (39,1)	494 (35,6)	0,061
3 or more	463 (36,4)	654 (47,2)	<0,001
Age ≥30 years at first full-term pregnancy, n (%)			
30 or more	270 (21,2)	161 (11,6)	<0,001
Less 30	1005 (78,8)	1105 (79,6)	0,591
Unknown	---	121 (8,8)	
Oral contraceptive use, n (%)			
Yes	223 (13,4)	644 (37,2)	<0,001
No	1435 (86,6)	958 (55,3)	<0,001
Breastfeeding (practice),n (%)			
Yes	841 (66,0)	1318 (95,0)	<0,001 *
No	434 (34,0)	1(0,07)	<0,001 **
Unknown	---	68 (4,93)	
** Test Z ** Fisher's exact test*			
Personal history of breast pathology, n (%)			
Dysplasia	26 (1,6)	227 (13,1)	<0,001
Atypical hyperplasia /CIS	21 (1,3)	36 (2,1)	0,0 66
Cancer	136 (8,2)	170 (9,8)	0,101
Family history of breast cancer, n (%)			
Yes	47 (20,9)	483 (27,9)	<0,001
No	1311 (79,1)	1162 (67,1)	<0,001

changes between the 1982 and the 2012 TNM systemfor BC [13] some differences can be point out in clinical stages of presentation (Table 2). In a strict comparison of stage versus stage, we observe: stages I of both series shows a non-significant difference (30, 6 % vs. 34, 5%); stage II of 1982-1983 series (43, 4%) was, statistically significant, more frequent than stage II (26, 1%) from 2012-2013 one. In those stages III that can be compared (IIIa and IIIb) there is a decrease, statistically significant, in the 2012-2013 series (IIIa: 14, 6% vs. 7, 6% and IIIb: 7, 4 vs. 3, 3 %). In stage IV, equally defined in the 1982 y 2012 TNM classifications, a no statistically significant (<0,051) decrease (3, 5 % vs. 2, 4%) was observed.If used as staging criteria that one defined as ***"early stage cancer"*** (0-IIIa) (Table 2) it is seen that there is almost no difference between the two series (88, 6% vs. 87,9%); on the contrary there is a reduction (statistically significant) in the later stages in the 2012-2013 series (10,9% vs. 6,3%).When applying the staging criteria of the 1982 TNM system in the 2012-2013 series (Table 3) statistically significant differences were observed with an increase of stage I and decrease of stages II and III in the series 2012-2013. On the contrary, the decrease in the percentage of cases in stage IV, in the most current series, is not statistically significant.

Histopathology

The percentages of non-infiltrative and infiltrative carcinomas show, both of them, statistically significant differences among 1982-1983 and the 2012-2013 series (Table 4). An increase of almost 5-fold in the diagnosis of non-infiltrating forms (2, 5% vs. 12, 0 %) is accompanied by a decrease (97, 5 % vs. 88, 0%) in the diagnosis of infiltrative forms in the 2012-2013 series.Given the lobular or ductal origin it is observed that in the non-infiltrating forms there was a decrease of nearly 7 times (21.0% vs. 3.4%) in the diagnosis of lobular variants in 2012-2013 series while the ductal variants showed an increase (79,0 % vs. 96,6 %) in the last set. In the infiltrating carcinomas there is an increase of nearly double in lobular variants diagnosis (6, 3 % vs.13, 7 %) with a decrease in ductal variants in the series 2012-2013 (93, 7 % vs. 87, 0 %). All mentioned above differences are statistically significant.

Diagnostic methodology

Breast self-examination (BSE):

More than half (53%) of the patients have no knowledge on the technique of self-examination in the 1982-1983 series; this ignorance is reduced 2.3 times (23%) in the 2012-2013 series being this reduction statistically significant. There is a, statistically significant, increase in the knowledge and practice between the two series (36, 6% vs. 47, 7 %). The knowledge and not practice also shows a statistically significant increase (10, 3%

Table 2: Breast cancer.Bilaterality and TNM Clinical stages. Comparative between 1983-84/2012-13 series

Variables	1983-84 (n 1658)	2012-13 (n 1732)	p
Bilaterality, n(%)			
Unilateral	1630 (98,3)	1679 (97,0)	<0,051
Bilateral	28 (1,7)	53 (3,0)	<0,051
TNM Clinical stages, n (%)			
0	-	162 (9,4)	-
I	507 (30,6)	598 (34,5)	<0,014
IIa	720 (43,4)	452(26,1)	<0,001
IIb	-	179 (10,3)	-
IIIa	242 (14,6)	131(7,6)	<0,001
IIIb	123 (7,4)	58 (3,3)	<0,001
IIIc	-	11 (0,6)	-
IV	58 (3,5)	41 (2,4)	<0,051
"Early stage cancer", n (%)			
0-IIIa	1469 (88,6)	1522 (87,9)	0,512
IIIb-IV	181 (10,9)	110 (6,3)	<0,001

Table 3: Breast cancer. TNM Clinical staging of both series by TNM System 3er Editon.1982.Comparative between 1983-84/2012-13 series

TNM Clinical stages (1982), n (%)	1983-84 (n 1658)	2012-13 (n 1732)	p
I	507 (30,6)	760 (43.9)	<0,001
II	720 (43,4)	631(36,4)	<0,001
IIIA	242 (14,6)	131(7,6)	<0,001
IIIB	123 (7,4)	69 (3,9)	<0,001
IV	58 (3,5)	41 (2,4)	0,051
Unknown	8(0,5)	100 (5,8)	<0,001

Table 4: Breast cancer. Histopathology. Comparative between 1983-84/2012-2013 series

Variables	1983-84 (n 1658)	2012-13 (n 1732)	p
Infiltration, n (%)			
Non infiltrative	42 (2,5)	209 (12,0)	< 0,001
Infiltrative	1616 (97,5)	1520 (87,9)	< 0,001
Unknown	---	3 (0,1)	
Non infiltrative, n (%)			
Lobular	9 (21,0)	7 (3,4)	< 0,001
Ductal	33 (79,0)	202 (96,6)	< 0,001
Infiltrative, n (%)			
Lobular	102(6,3)	198 (13,0)	< 0,001
Ductal	1514 (93,7)	1322 (87,0)	< 0,001

Table 5: Breast cancer. Diagnostic methodology. Comparative between 1983-84/2012-2013 series

Variables	1983-84 (n 1658)	2012-13 (n 1732)	p
Breastself-examination,n (%)			
Notknown	879 (53,0)	411 (23,7)	< 0,001
Knows and does not practice	171 (10,3)	316 (18,2)	< 0,001
Knows and practices	602 (36,3)	827 (47,7)	< 0,001
Unknown	6(0,4)	178 (10,4)	
Clínical examination (practice), n (%)			
Yes	1582 (95,4)	1568 (90,5)	< 0,001
No	39 (2,4)	12 (0,7)	< 0,001
Unknown	37 (2,2)	152 (8,8)	
Clínical examination (result), n (%)			
Positive	1534 (96,9)	1244 (79,3)	< 0,001
Negative	48 (3,1)	324 (20,7)	< 0,001
Mammography (practice), n (%)			
Yes	1366 (82,4)	1630 (94,1)	< 0,001
No	255 (16,4)	91 (5,2)	< 0,001
Unknown	37 (1,2)	11 (0,7)	
Mammography (result),n (%)			
Positive	1244 (92,0)	1232 (75,7)	< 0,001
Negative	122 (8,0)	371 (22,7)	< 0,001

vs. 18, 2%) (Table 5).

Clinical examination (CE):

When the frequency of the practice of clinical examination (Table 5) in the diagnosis of BC is compared a decrease, statistically significant, in the 2012-2013 is seen (95, 4% vs. 90, 5%); It is also observed in this series a decrease, statistically significant, in the positive results of this test (96, 9% vs. 79, 3%).

Mammography:

The practice of mammography in the BC diagnosis, showed a statistically significant increase in the 2012-2013 series (82, 4 % vs. 94, 1 %) (Table 5). For the analysis of resultsin the 2012-2013 series only the BI-RADS 4 and 5 diagnosis were considered as positive. Under this condition a decrease is observed in the positive results (92, 0 % vs. 75,7 %) in the 2012-2013 series; by contrast negative results in the same series are increased almost three times (8,0 % vs. 22,7 %) being in both cases statistically significant differences.

Discussion

According to the World Bank Argentina, situated in South America, belongs both to the "Less developed regions" and to the "Medium human development" group of countries [14] where BC's estimated incidences are of 31, 3x100, 000 and 26, 5x100, 000 respectively [1]. Despite these two categories and its geographic location Argentina is strikingly present among the countries with a high incidence rate for BC (71, 2 per 100,000). This difference in the incidence of BC with the rest of the region is a fact that has been observed over the last 40 years [15-18].

The persistent high incidence rates led us to raise the question of whether the clinical and epidemiological BC's profile remains the same or has been modified as a result of changes in women habits and customs or in their environments that occurred, mainly, in the second half of the past century [19,20]. As they were at our disposal data from a series of BC (1658 cases) reported between 1982-83 we decided to compare them with the results of a series (1732 cases) of cases reported between the years 2012-13.The variables evaluated in both studies were compared settling down the statistical significance of the differences observed.

Age distribution

Despite the assertion that BC is a leading cause of death and disability among women, especially young women [21,22] and that the BC occurs increasingly in younger women in developing countries [23-26] we found striking data regarding age at diagnosis when we compare both series.There is a clear similarity in the percentage of cases by age group from under age 44 until 65-74 years old group; moreover, although not statistically significant, there are a slight predominance of younger women (between 40-44 years and 65-74 years groups) in the 1983-1984 series.It is in the group of women over age 75 where a significant increase of cases in the 2012-2013 series is observed. This increase can be understood, partly, by the increase in both life-expectancy (at birth and at age 60) observed in the female population over the last 30 years[27].On the other hand, increased use of mammography in the last 30 years takes to older women to have a mammogram [28-30] even against the recommendations of international medical societies and health authorities regarding the upper age limits for screening [31-33]. This would allow more BC grouped under the concept of "overdiagnosis" to be diagnosed [34-36].

Risk and protective factors

In the study and comparison of the gynecologic and the reproductive history of patients of those variables considered as "risk factors" or as "protective factor" for BC in both series we find striking similarities in the gynecologic history of patients. In both almost 2/3 of the BC corresponds to menopausal women; there is also a coincidence in the age of menarche. These two data show that both series are quite comparable to each other and with most reported worldwide series from "western societies" [37]; it, also, allows us to suppose that they would be BC cases due, mainly, to recognized hormonal risk factors [38,39]. In the reproductive history of patients there is also a remarkable similarity inthe percentage of nulliparous women; this recognized and accepted "risk factor" is strongly associated with BC in postmenopausal women [40,41] as are most of the patients in both series. Age ≥30 years at first full-term pregnancy, another accepted "risk factor" shows a marked decrease, near the half, in the most recent series although the percentages are low in both series compared with published data [41,42]. Considering the number of children born alive as a protective factor [43,44] we see that number of 2 children was and is the most common;this data is consistent with the average number of children obtained in population censuses near the years in which the studies were conducted. The decrease in group 1 child observed in the 2012-2013 series is offset by the increase in the group of 3 or more children seen in the same series. Indirectly related to all the factors described is the use of OC. The increase of 2.8 times of patients using oral contraceptives (OC) in the 2012-2013 series is a worrying fact but we should keep in mind that when the cohort of women, in the 2012-2013 series, was at ages of reproduction the OC use as a method of familiar planning [45] was widespread among us and its adverse effects were less known and studied than at present [46]. The practice of lactation is currently considered as one of the most proven protective factors against BC [47,48]. Regarding this we observed a significant and beneficial increase (1.5 fold) of its practice in the 2012-2013 series. This is due mainly to the preaching in the last 3 decades of the benefits, both for the baby and mother, of breastfeeding. Both national and international medical societies, non- governmental organizations and the representatives of public health [49] sponsor this preaching. However today is more valued as a protection factor the total time of breastfeeding of all breastfed children [50]. This data we have it available in the 2012-2013 series but not in the 1982 - 1983 series reason why we only evaluate practice as yes or no. Moreover, in the most recent series the average time of breast-feeding was 6 months [11] a value below the recommended for practice of breast-feeding as a protective element for BC [50]. All the variables of reproductive history previously mentioned are also related, directly or indirectly, to socio-cultural factors.

Breast cancer history

When personal history of breast cancer was studied no differences were found while in the family history, are cognized risk factor [51-53], an increase was observed. Also no differences were found in the history of the so-called pre-cancerous or potentially malignant lesions [54, 55] such as Atypical Hyperplasia and CIS.

TNM Clinical stages

As indicated in the results, the comparison between the presentation stages in both series required some qualifications to be performed. The main differences between the 1982 and 2012 TNM system for BC were the introduction of category 0 and the split of categories II and III. As there was no stage 0 in 1982 Stage System this kind of lesions, when diagnosed, were included in stage I ; in categories II and III new subcategories (IIb and IIIc) were incorporated into theTNM system used in 2012. When the criteria of 1982 TNM system are applied to the 2012- 2013 set a relative equivalence is obtained allowing us a somewhat stricter comparison between the series. Thus the differences become more evident with significant increases of the more initial stages, remaining stage IV without significant differences; this undesirable result in the presentation stage would show that the advanced stages presentations correspond more to the aggressive biology of the tumors [56] than to the application of the current diagnostic methodologies and the carrying out of screening campaigns for BC.

Morphology

In both series bilateralism corresponded to those clinical carcinomas diagnosed in simultaneous in both breast at the time of the first consultation or during the routine mammographic screening of the contralateral breasts of patients with unilateral disease within an interval of 6 month (synchronous bilateral breast carcinoma, SBBC). The bilaterally in itself had a negative impact on prognosis [57]. In the 1983-1984 series, the percentage of 1.69% of SBBC was high compared with data published at that time [58]. The percentage of 3% in the 2012-2013 series while

higher, with no obvious statistical significance if compared to the previous series, it is also high for the percentages reported today [59]. To explain, in part, this increase we must consider the increased sensitivity of the methods used today for the study of the contra-lateral breast [60].

Regarding histology there is a marked increase in the diagnosis of non-infiltrating forms with a consequent reduction of infiltrating variants in the 2012- 2013 series. This increase is also observed globally [61]; our data in relation to the increase of the non-infiltrating forms are very coincident with those reported in a US series that reported a fivefold increment of the frequency of non-infiltrative forms, mainly ductal, in the past 25 years [62,63]. Pure DCIS accounts for 15 to 20% of breast cancers compared with only 5% of cases before the advent of breast cancer screening [64, 65]. The declining percentage of infiltrating ductal carcinoma seems likely due to the introduction of new codes, which allowed combination diagnoses of infiltrating ductal carcinoma with other histology [66]. Decreases in use of combination estrogen-progestin menopausal hormone therapy (EPHT) [67, 68], treatment of in situ cancers and saturation or decline in systematic mammography screening have both been postulated as a cause for the decrease in overall breast cancer incidence [69]. There is growing evidence that the increased risk of breast cancer associated with EPHT use is higher for invasive lobular and invasive lobular-ductal mixed tumors than for invasive ductal carcinoma [70]. Although not as common as DCIS, lobular carcinoma *in situ* (LCIS) incidence rates also increased -4fold from 1978 to 1998, with the highest increase observed among women ages 50 years and older [71,72]. However, unlike ductal carcinoma, lobular breast cancer is not detected primarily through mammography but it can be incidentally detected with an increase in biopsies resulting from the use of mammography [61 73]. All previously mentioned can be applied to the explanation of the data obtained in the comparison of our two series.

Diagnostic methodology

For more than a decade studies have shown that breast self-examination and breast physical examination play a small role in finding breast cancer[73] and are unhelpful in reducing stage at diagnosis and mortality [74]**.** Although aware of the limitations of these diagnostic methods, they were studied in both series because they are, indirectly, indicators of the degree of concern regarding breast cancer among patients. There is a remarkable increase (2.3–fold) in the knowledge of the BSE due to the campaigns carried out, during the last decades, mainly by non-governmental organizations dedicated to the topic of breast cancer. While there was an increase of the number of women who know and do practice BSE paradoxically so did the number of women who know and do not practice.Regarding the practice of the clinical examination and the positive results a decrease of both in 2012-2013 series is observed; the main explanation for these results is that at present most of the BCs are diagnosed in sizes smaller than the sensitivity of this method and that the diagnosis is increasingly based on the findings of the imaging methods (mammography and ultrasound) [60]. The practice of mammography, although was high in both series, showed a significant increase in the 2012-2013 series reaching almost 95%. This percentage of practice resembles those reported in BC series of developed countries [75]. Given the non-existence until 1992 of the BI-RADS system for mammography report [76] a comparison of the results was possible only if it is assumed that in the 2012-2013 series were regarded as positive those cases diagnosed as BI-RADS 4-5 on the first report being considered all the remaining categories negatives.

Conclusions

The comparative study of two cohorts of women from a single geographical location with breast cancer and separated in time by what is defined, sociologically and biologically, as a generation (30 years) showed some striking results.

These are two cohorts of mostly menopausal women with a nearly equal incidence age (59 years); the incidence curve according to age groups shows a remarkable overlap from the age of 40 to 75 years. Compared the age of menarche and menopause, there is another remarkable similarity between the two populations. Those postulated "risk factors" related to cultural behaviors such as use of oral contraceptive (OC), parity and lactation showed certain differences: there was increased use of OC.; the number of two children remained the same with an increase of 3 or more children; primiparous women over 30 years of age declined and breastfeeding was more practiced. The differences observed between the two series in terms of histological forms, in situ / infiltrating and ductal / lobular, are the same as those reported worldwide mainly in "western" populations.

Everything mentioned in the previous paragraphs makes us think of two very similar cohorts of patients with BC more related to hormonal factors and coming from "western" societies with a high level of human development; they seem to come, apparently, from the same population and not from two separated by 30 years populations. If one considers our population cultural and genetic background, with a strong European component, the expected change in the presentation's profile of the female BC seems to need more than one generation to occur and to resemble that one of the geographic region in which we are located (South America) and the levels of "Less developed regions" and "Medium human development "we have achieve as a country. Nevertheless, this change may take less time to produce if we take into account the main source of new migrant populations in recent decades. Most of them come from neighboring countries (Brazil, Uruguay, Paraguay, Chile and Bolivia) or nearby in South America (Peru and Colombia) [77]. If we consider the incidence rates of BC in these countries we observe a median of 35.7x 100.000 with a range of 19.2 (Bolivia) and 69, 8x100.000 (Uruguay)(1). All previously mentioned countries differ with ours in the ethnic composition of their populations, with a higher prevalence of Amerindians and/or Afro-descendants inhabitants.

Perhaps future research on population genetics and BC could show if assimilation of these foreign populations into the cultural and genetic background of our current population could mean a decrease in the incidence rates of female BC and an increasing resemblancein the presentation profile tending to that ofthe geographical region in which we are located and the human development level achieved as a society.

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