Epidemiology of Breast Cancer at the Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan

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ABSTRACT

Objective: To describe the demographic and clinical features of females presenting with breast malignancies at the Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH & RC), Lahore, Pakistan.
Study Design: An observational study.
Place and Duration of Study: SKMCH and RC, Lahore, from January 2008 to December 2012.
Methodology: Demographic and clinical features of female breast cancer patients, registered at SKMCH and RC, were studied. Mean values, counts, and percentages were obtained.
Results: Four-thousand, three-hundred and sixty-six female breast malignancies were recorded. Nearly 80.4% of the patients belonged to Punjab. Mean age at presentation was 48.6 ±12.2 years, at menarche was 13.2 ±1.2 years, and at first childbirth was 23.7 ±4.8 years. Mean Body Mass Index (BMI) was 29.0 ±5.7 kg/m^2. In 60.1%, history of breast feeding was positive. In 55.7%, there was no history of use of any Oral Contraceptive Pills (OCP)/Hormone Replacement Therapy (HRT). Nearly 42.7% were postmenopausal, 85.2% had infiltrating ductal carcinoma, 49.6% had grade 3 tumor, 60.7% had stage II disease, and 37.3% were Estrogen Receptor (ER)/Progesterone Receptor (PR)+, Human Epidermal Growth Factor Receptor 2 (HER2)-. Family history of breast cancer was positive in 16.9% of the cases.
Conclusion: The mean presenting age is lower than what has been recorded in the West. It may be worthwhile collating results from different institutions in order to study the epidemiology of the disease more extensively and develop cancer control and early detection programs.

Key Words: Breast cancer. Grade. Stage.

INTRODUCTION

In the year 2012, the annual Age-Standardized Incidence Rate (ASIR) for breast cancer stood at: 43.3/100,000 females at a global level and at 50.3/100,000 in Pakistan.[1] Further, for the time period from 2006 - 2010, the Surveillance, Epidemiology, and End Results' (SEER) Program has shown that, per 100,000 women, the ASIR was 123.8 for all races combined, 127.4 for White, 121.4 for Black, 91.8 for Asian/Pacific Islander, 90.8 for Hispanic, and 77.1 for American Indian/Alaska Native.[2] Moreover, in the United Kingdom, in 2010, the ASIR stood at 125.9 per 100,000 women,[3] whereas, in Australia the rate has remained fairly stable over the years, with the rate in 2009 equaling 113.5 per 100,000 women.[4] The rates in the recent years in the most advanced countries of the world vary from being moderately high to very high.

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Shaukat Khanum Memorial Cancer Hospital and Research Center is a complete cancer treatment facility established in 1994, in Lahore, Pakistan. A total of 11,853 breast cancers were recorded in all age-groups, both gender combined in an 18-year time period between December 29, 1994 and December 31, 2012.[5]

The objective of this study was to describe the demographic and clinical features in female breast cancer patients registered at the Hospital from 2008 to 2012.

METHODOLOGY

An observational study was conducted in 2013 - 2014 at the Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore. This was done through a retrospective review of the medical records of the registered patients. Breast malignancies coded from C50.0-C50.9 using the ICD-O-3 classification scheme were studied.[6] Information was collated on variables recorded between January 2008 and December 2012 (5-years).

The variables included the demographic features as the geographic area of residence, age at menarche, parity, age at first childbirth, number of children, breast feeding, use of oral contraceptives or hormone replacement therapy, menopausal status, weight, height, BMI, and family history of cancer. The clinical features included age at disease presentation, histology, tumor grade,

stage of the disease, and hormone receptor status (ER, PR, and HER2/neu). Grade was classified according to the ICD-O-3 classification.[6] Stage was grouped using the American Joint Committee on Cancer staging schemes.[7-8] The hormone receptor status was combined to create four categories,[9] as described in the West. Immunohistochemistry was performed to determine the HER2/neu status. In cases where the test was equivocal, receptor status was confirmed through HER2/neu gene amplification using fluorescent *in-situ* hybridization. For this study, if any other family member had breast cancer, regardless of whether it was a first-degree or a second-degree relative, family history of breast cancer was taken as being positive. Another category included was a family history of cancer other than breast cancer.

The Statistical Package for Social Sciences (SPSS) software, version 19, was used to conduct the analysis and descriptive results were presented. For continuous variables, mean, standard deviation, and range were computed. Continuous variables included age at presentation, age at menarche, age at first childbirth, weight, height, and BMI. Counts and percentages were presented for categorical variables, which included family history of cancer, parity, children, breast feeding, use of OCPs/HRT, menopausal status, histology, grade, stage, and ER/PR/HER2 status. The Institutional Review Board was informed about the study and exemption from full review, granted as the study was retrospective in nature and information being presented was without any personal identifiers.

RESULTS

During a 5-year time period between January 2008 and December 2012, a total of 4,411 cases of breast cancer were recorded in the Registry, accounting for 20.4% of all malignancies. Of these, 4,366 (99%) were seen among female patients and 45 (1%) in male patients. A detailed analysis of the data of these female patients was conducted to obtain information on the demo-graphic and clinical features of the patients (Table I). Of the 4,366 patients, province-wise, 3,509 cases (80.4%) belonged to Punjab, 473 (10.8%) to Khyber Pakhtunkhwa, 192 (4.4%) to Sindh, whereas, the remaining 192 (4.4%) were from all other regions of the country and Afghanistan. Further, of the 4,366 cases, the district of residence of most of the females was Lahore, (1,601 (36.7%), followed by Faisalabad (241 (5.5%)) and Gujranwala (226 (5.2%)), with the distributions for other 84 districts combined being about 52.6%.

The mean age at menarche was 13.2 ±1.2 (9 - 25 years) and at first childbirth was 23.6 ±4.9 (11 - 44 years). Among the 3,777 in whom the parity was noted, on an average, females had 4 children (1 - 15). History of OCP/HRT use was present in 9.4% of the cases, there

Table I: Demographic and clinical features of females with breast cancer at SKMCH and RC, 2008-2012.

Variables	Mean±SD (range)	Median
Age at presentation (years) (n=4,366)	48.6 ±12.2 (6-91)	48.0
Age at menarche (years) (n=2,842)	13.2 ±1.2 (9-25)	13.0
Age at first born (years) (n=2,055)	23.7 ±4.9 (11-44)	23.0
Weight (kg. (n=4,284)	69.5 ±14.1 (20.0-158.4)	68.4
Height (cm. (n=3,998)	154.8 ±5.9 (126.0-184.0)	155.0
BMI (n=3,998)	29.0 ±5.7 (12.6-64.1)	28.6

	Number	Percent
Family history of cancer (n=4,366)		
Breast cancer (n=4,060)		
Present	737	16.9
Absent	2,760	63.2
Unknown	563	12.9
Other cancers (n=306)	306	7.0
Parity (n=4,366):		
Yes	3,332	76.3
No	445	10.2
Unknown	589	13.5
Children (n=4,366):		
Yes	3,332	76.3
No	445	10.2
Unknown	589	13.5
Breast feeding (n=4,366):		
Yes	2,624	60.1
No	501	11.5
Unknown	1,241	28.4
Use of OCPs/HRT (n=4,366):		
Yes	411	9.4
No	2,433	55.7
Unknown	1,522	34.9
Menopausal status (n=4,366):		
Pre-menopausal	1,819	41.7
Postmenopausal	1,866	42.7
Unknown	681	15.6
Histology (n=4,366):		
Ductal	3,781	86.6
Lobular	202	4.6
Mixed (ductal, lobular)	51	1.2
Carcinoma, NOS	107	2.4
Others	225	5.2
Grade (n=4,366):		
1	55	1.3
2	1,806	41.4
3	2,164	49.6
Unknown	341	7.8
Stage (n=4,366):		
0	90	2.1
1	273	6.3
2	2,652	60.7
3	743	17.0
4	186	4.3
Unstageable	422	9.7
ER (n=4,366):		
Positive	2,709	62.0
Negative	1,495	34.2
Unknown	162	3.7

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Table I continues:

PR (n=4,366):		
Positive	2,196	50.3
Negative	1,999	45.8
Unknown	171	3.9
HER2 (n=4,366):		
Positive	1,072	24.6
Negative	2,353	53.9
Equivocal	594	13.6
Borderline	4	0.1
Unknown	343	7.9
ER,PR,HER2 (n=4,366):		
ER/PR+,HER2+	596	13.7
ER/PR+,HER2-	1,627	37.3
ER/PR-,HER2+	476	10.9
ER/PR-,HER2-	723	16.6
Unknown	944	21.6

was none recorded in 55.7% of the cases, and it was unknown in 34.9% of the cases. Menopausal status included 41.7% pre-menopausal and 42.7% post-menopausal women, with the status being unknown in 15.6% of the women. BMI was recorded in 3,998 cases; of these, 1.7% had a BMI less than or equal to 18.5, nearly 23% had a normal BMI (18.4 - 24.9), 30% had an elevated BMI (25.0 - 29.9), whereas, the rest were obese with a BMI of 30 or greater. Family history of any type of cancer was present in 1,043 cases (23.9%), absent in 2,760 (63.2%), and not recorded in 563 (12.9%) cases. Family history of breast cancer was recorded in 737 (16.9%) of the females and a family history of both breast and ovarian cancer was found in 6 cases (< 1%).

As for the clinical features, the mean age at presentation was 48.6 ±12.2 (6 - 91; median 48 years). Approximately 23% of the females were under age 40 years, 71% in the age-group 40 - 69 years, and 6% equal to older than 70 years of age. Distributions for histology revealed that about 86.6% of the cancers were ductal carcinomas, with 85.2% being invasive in nature and 1.4% were *in situ* (63/4,366); 4.6% were lobular carcinomas, with 4.58% being invasive in nature and 0.02% *in situ* (2/4,366). The grade distribution of the tumors included: grade 1 (well differentiated) 1.3%, grade 2 (moderately differentiated) 41.4%, grade 3 (poorly differentiated) 49.6%, and the grade could not be determined in 7.8%. The stage distribution was as follows: stage 0 - 2.1%, stage I - 6.3%, stage II - 60.7%, stage III - 17.0%, and stage IV - 4.3%. Nearly 9.7% of the cancers could not be staged. The commonest ER/PR/HER2 distributions were for ER/PR+, HER2- (37.3%), followed by ER/PR-, HER2- (16.6%), ER/PR+, HER2+ (13.7%) and ER/PR-, HER2+ (10.9%).

DISCUSSION

Although it cannot be considered to be representative of the population of the country, this large cohort of breast cancer patients from SKMCH and RC, as it represents one of the largest cohorts of breast cancer patients from any single institution in Pakistan. The mean age at presentation in this study was 48.6 years. Other studies in the region have reported the mean age to be almost the same, approximately 48 years (21 - 87 years).[10] In Iran, the mean age has been reported to be around 51.3 years,[11] whereas, in India, it has been stated to be about 51 years.[12] The mean presenting age in American studies has been documented to be around 54.2 years (African-Americans) and 60.4 years (Caucasians).[13] Additionally, in the United Kingdom, one study has reported the mean age for women to be around 64 years,[14] while in Australia, it has been confirmed to be 60.7 years.[4] All these reports support that the finding that the mean presenting age in Pakistan is lower than what has been seen in other parts of the world, including the neighbouring country of India.

As regards the histologic diagnosis, in this study, infiltrating ductal carcinoma was considered to be a common finding; similar findings have been reported in other studies.[10] Moreover, over 21% of the cases were diagnosed in an advanced stage in the natural history of the disease (stages III-IV). A study from another leading cancer treatment hospital in Lahore has reported the figure for stages III-IV disease to be close to 70%.[10] This difference in the figures might be because of the difference in the policy related to patient acceptance for treatment at these institutions. Nevertheless, it may be worth considering early detection of the disease so as to downstage the cancers and improve the quality of life of patients suffering from this disease.[15] A figure of 21% in stages III - IV in this study is markedly different from a figure of 5% of cancers with distant metastasis seen in America for women with breast cancer.[16] This study further shows that most cancers have a high grade. Other studies have also revealed that most cancers are poorly differentiated.[10,17] A study conducted in America on the Asian-Indian/Pakistani group with breast cancer showed the presenting age to be younger than what is seen in the West, higher stage, higher grade, and more hormone receptor negative disease.[18,19] As for the hormone receptor status (ER, PR, and HER2), studies have shown a significant proportion of the cancers to be hormone receptor negative type.[17] This is consistent with what has been found in this study. One study has also found the ER status to be significantly associated with the disease free survival.[20]

Family history of cancer was present in about 24%, and absent in nearly 63% of the total patients. Although, information related to family history of all the cases has not been recorded, the vast majority of cancers appeared to be sporadic in nature. Studies have reported the family history of cancer, single marital status, and older age at menopause to be associated with an increased risk of breast cancer for women.[21,22]

Not only this, nulliparity, having few children, post-menopausal status, the use of oral contraceptives, and a family history of breast cancer were found to be associated with breast cancer but the age at menarche was not.[23,24] Further, one study from Morocco has shown that familial breast cancer seems to affect young women and tends to present high Scarff-Bloom-Richardson grade tumors with lymph node involvement, with absence of progesterone receptors.[25] Conducting extensive epidemiologic studies to review various factors including the family history of cancer could highlight the importance of sporadic cancers and implementing programs for downstaging the disease among women presenting with sporadic cancers.

CONCLUSION

The female breast cancer patients had a lower mean age (48 years) at presentation compared to what has been reported in the advanced countries of the world, age at menarche was 13.2 years, age at first childbirth was 23.7 years, and the BMI was on the higher side. Family history of breast cancer was positive in less than 1/5th of the patients, majority of the females were parous and had breast-fed their children, most had not used any OCPs/HRT. The difference in the pre- and postmenopausal status was not significant. Moreover, many women had infiltrating ductal carcinoma, grade 3 tumor, stage II disease, and ER/PR+, HER2- cancers.

At present, we rely heavily on the data from the West to enlist factors that could be implicated in the etiology of various diseases including breast cancer. Conducting large studies, at a population-level, could assist in highlighting the plausible risk factors within our population. Therefore, various institutions should consider putting together their data on breast cancer, to conduct studies bigger than this one, in an attempt to determine the potential risk factors and, also the incidence of breast cancer in a definite time period, within a specified population, living in a well-defined geographic area, which could be the district of Lahore. Breast cancer being a common diagnosis in Pakistan, this type of epidemiologic study is worth considering. This could further assist in designing programs for early detection and cancer control in the region.

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