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Epidemiology, Pathology and Histochemistry Features in Women with Breast Cancer

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Abstract **Background:** Breast cancer is the most frequent malignancy among women and is the leading cause of death through middle-aged women. Despite the high frequency of breast cancer among Iranian women, the epidemiological characteristics of breast cancer among Iranian patients are yet unknown. Herein, we investigate epidemiology, pathology and histochemistry features in women with breast cancer in Iran. **Materials and Methods:** Between of 2002 to 2012, 546 patients with breast cancer, who were referred to Rasool-Akram Hospital, Tehran, Iran were studied. They were surveyed for age, size of tumor, family history of disease, laterality, type of pathology, grade, stage, tumor markers and metastasis. **Results:** The mean age of patients at diagnosis was 46.8 ±11 years. Size of tumor in 113 patients (20.7%) was 0.1-2 cm, 349 patients (63.9%) between 2.1-5 cm and 84 patients (15.4%) >5 cm. Forty-seven patients (8.6%), 382 patients (70%) and 117 patients (21.4%) had grade I, grade II and grade III, respectively. 185 patients (33.9%) had metastasis (35 patients at diagnosis and 150 patients in time of treatment) to other organs. 538 patients (98.5%) didn't have family history of ovarian cancer and also 501 patients (91.8%) didn't have family history of breast cancer. **Conclusions:** The mean age at diagnosis of BC in Iran is around 46 to 49 years. Tumor size in our study is lower than many studies. The organ as site of the most metastases was the lung in our patients, while in other studies it is the bone.

Keywords: *breast cancer, epidemiology, pathology*

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1. Introduction

Breast cancer (BC) is the most common cancer (27% of all cancers) and also the leading cause of death (16%) due to cancer in women, both in developed and developing countries [1]. BC is the most frequent malignancy among Iranian women. However the epidemiological features of BC among Iranian patients are yet unknown [2]. Even after adjusting for age, most of Iranian patients are at least one decade younger than their western counterparts and present with advanced stages of disease [3]. In Asia the maximum incidence for BC is in the 40 – 50 year old age groups [4]. Aging is considered as one of the main risk factors for developing new BC events and it is known that 50% of BC occurs in women ≤65 years and more than 30% in women ≤70 years in developed nations [3]. BC starts as a local disease, but it can metastasize to the lymph nodes and distant organs [5].

In this study, we investigate epidemiology, pathology and histochemistry features in women with BC in Iran. These findings can provide basic data about BC in Iran, it may be appropriate to utilize the findings of this study for developing long-term strategies to reverse the increasing trend of BC in Iran and other developing countries

2. Materials and Methods

2.1. Patients

Between 2002 and 2012, 546 patients with BC were referred to Rasool-Akram Hospital, Tehran, Iran. We studied age, size of tumor, family history of disease, laterality, type of pathology, grade, stage, tumor markers and metastases in all patients. ER and PR positivity was defined as ≥10% positive tumor cells with nuclear staining. HER2 positivity was defined as either HER2 gene amplification by fluorescent *in situ* hybridization or scored as 3+ by IHC. In case of HER2 2(+), fluorescent *in situ* hybridization was performed to determine HER2 positivity. Triple negative BC was defined as ER (-), PR(-), and HER2(-).

2.2. Statistical Analysis

The graphs were plotted in Excel 2007 software and correlation between variables was done by IBM SPSS statistics 19 software (T-test and Chi square). P≤0.05 was statistically significant.

3. Results

Table 1. The basic variables at diagnosis in the patients with breast cancer(N=546)

Variables	N(%)	Mean±SD	Range
Age(year)		46.8±11	19-85
Sex			
Male	0(0)		
Female	546(100)		
Size of Tumor(cm)			
0.1-2	113(20.7)		
2.1-5	349(63.9)		
>5	84(15.4)		
Family History of Ovarian Cancer			
Yes	8(1.5)		
No	538(98.5)		
Family History of Breast Cancer			
Yes	45(8.2)		
No	501(91.8)		
Laterality			
Unilateral*	528(96.7)		
Bilateral**	18(3.3)		
Type of Pathology			
Invasive ductal carcinoma	511(93.6)		
Invasive lobular carcinoma	32(5.9)		
Others	3(0.5)		
Histological Grade			
I	47(8.6)		
II	382(70)		
III	117(21.4)		
Stage			
I	48(8.8)		
IIA	151(27.6)		
IIB	116(21.2)		
IIIA	135(24.7)		
IIIB	15(2.8)		
IIIC	46(8.5)		
IV	35(6.4)		
Metastasis			
Yes	185(33.9)		
No	361(66.1)		
Type of breast cancer			
Triple negative	86(15.7)		
Non-triple negative	460(84.3)		

*Right or Left breast **Both (right and left breast)

The mean age of patients at diagnosis was 46.8±11 years (Range, 19-85 years). All patients were female (Table 1). Out of 546 patients, size of tumor in 113 patients (20.7%) was 0.1-2 cm, 349 patients (63.9%) between 2.1-5 cm and 84 patients (15.4%) >5 cm. 538 patients (98.5%) didn't have a family history of ovarian cancer and also 501 patients (91.8%) didn't have a family history of breast cancer. 528 patients (96.7%) had involvement in right or left breast and 18 (3.3%) in both breasts. Type of pathology for 511 patients was invasive ductal carcinoma, for 32 patients (5.9%) was invasive lobular carcinoma and for 3 patients (0.5%) were other histologies. 47 patients (8.6%), 382 patients (70%) and 117 patients (21.4%) had grade I, grade II and grade III, respectively. 48 patients (8.8%), 151 patients (27.6%), 116 patients (21.2%),135 patients (24.7%), 15 patients (2.8%), 46 patients (8.5%) and 35 patients (6.4%), had stage I, stage IIA, stage IIB, stage IIIA, stage IIIB, stage IIIC and stage IV, respectively. A total number of 185 patients (33.9%) had metastases (35 patients at diagnosis and 150 patients during further treatment) to other organs (lung, bone, liver and brain were the most common sites of metastases, respectively). Of all patients, 86 patients (15.7%) were triple negative and 460 patients (84.3%) were non-triple negative.

4. Discussion

BC is the most frequent malignancy among women that can be a leading cause of death through middle-aged women [6]. Despite the fact that BC is a major health issue, very few studies describe its characteristics in the Middle East [7].

Table 2 shows number of patients and age in the patients with BC in Iran [4,8,9,10,11]. The mean age for BC patients in Iran are close to each other (around 46-49 years) and also range of age in these studies is 16-85 years.

Table 2. Number of patients and age in the patients with breast cancer in Iran

Reference	Area of study	Number of patients	Mean age(year)	Range(year)
4	West	133	46.3	24-78
8	Northwest	902	48.3	16-85
The presentation Study	Center	546	46.8	19-85
9	Center	303	48.2	24-84
10	Center	286	47.5	24-81
11	Northwest	140	47.6	-

A study in Pakistan on 2666 BC patients reported that the mean age ± standard deviation of the patients was 47.57 ±12.026 years and median age was 45 years and also range was 16 to 100 years [12]. A study in lebanon [7] reported the pathological characteristics of 624 patients diagnosed between 1990 and 2013 and showed that the mean age at diagnosis was 54.6±13.4 years. Age range of the patients in an Indian study was between 22-75 years (mean age, 47 years) [13]. The mean age and range in other areas of the world is similar to Iran.

A study on neo-adjuvant chemotherapy in the US [14] on 153 BC patients reported that the clinical stage at diagnosis was IIA in 22%, IIB in 28%, IIIA in 39%, and IIIB in 11%. Tumor size distribution was less than 2 cm in 5 patients (3.2%), 2.1-5 cm in 100 patients (65.3%), and greater than 5.1 cm in 48 patients (31.5%). Wong et al. [15] reported that the median tumor size at presentation for 1480 Southeast Asian women with BC was 3cm. Laudico et al. [16] showed that the average of stage distribution for the patients in Philippines from 1993 to 2002 was: I=5%, IIA=20%, IIB=18%, IIIA=9%, IIIB=10%, IV=11%, Unknown=28%. The study in Pakistan [12] reported that, what the primary tumor size is concerned, 1663 (62.4%) patients had a tumor>5 cm. Only 101 (3.8%) patients presented with a tumor up to 2 cm in size. Mean tumor size ± SD was 6.65 cm ± 3.08 cm. The study in Lebanon [7] showed that One third of the tumors had a size of more than 2 cm at diagnosis. In our study, Stage I, stage IIA, stage IIB, stage IIIA, stage IIIB, stage IIIC and stage IV were for 48 patients (8.8%), 151(27.6%), 116(21.2%), 135(24.7%), 15(2.8%), 46(8.5%) and 35(6.4%), respectively. Also, the size of tumor in 113 patients (20.7%) was 0.1-2 cm, 349 patients (63.9%) between 2.1-5 cm and 84 patients (15.4%) >5 cm. In the Indian study [13], average tumor size was 5 cm. In a recently published Iranian study [3], Stage I was diagnosed in 18%, stage II in 57% and stage III in 25% of BC patients and about 72% of the patients were diagnosed

with a tumor over 2 cm. These results show that tumor size in center of Iran (our study) is similar to other studies and stage distributions in studies are not the same.

The Lebanese study [7] reported that the triple negative subgroup constitutes only 8.3% in BC patients. Kennecke et al. [17] reported that the triple negative subgroup was 8.5% and non-triple negative was 91.5% in tissues from 2985 patients. In our study, the triple negative subgroup is 15.7% meaning that the triple negative subgroup in our study is more than other studies.

The infiltrative ductal tumors develop in breast ducts and represent 80% of tumors, the lobular tumors develop inside the lobes and account for 10 to 15% of cases and other subtypes represent less than 10% of cases diagnosed per year [4]. In the Indian study, out of the 120 cases, there were 113 cases(94.1%) of ductal carcinoma [13]. Infiltrative ductal carcinoma was found to be the most common at 77% and lobular carcinoma the least at 5%. Mousavi et al. [2] reported that ductal carcinoma in their study was 93.6% and lobular carcinoma was 5.9%. These results confirmed that ductal carcinoma is the most common subtype in BC and is more than 80%.

Out of the 120 cases in the Indian study, 5 (4.17) were grade I, 91 (75.83) were grade II, and 24 (20%) were grade III [13]. In our study, 47 patients (8.6%), 382 patients (70%) and 117 patients (21.4%) had grade I, grade II and grade III, respectively. Therefore, grade II is the most common grade and grade I is the least common grade in BC.

In a study in the US, metastatic disease developed in 145 of the 558 patients and the most common first site of distant spread was bone (51%), followed by lung (17%), brain (16%), and liver (6%). The remaining 10% of patients had multiple metastatic sites [18]. The four most common anatomic sites of distant metastases as the first exclusive event were bone (41.1%), lung (22.4%), liver (7.3%), and brain (7.3%) [19]. In our study, lung, bone, liver and brain were the most observed metastases, respectively. We can say that in this study, lung metastasis is more than other studies.

Following the identification of BRCA1 and BRCA2, screening tests were developed to identify mutation carriers and families at risk for hereditary breast and ovarian cancer [20]. Lifetime risk of developing BC for a woman with one or two first degree relatives affected with ovarian cancer is estimated to be approximately 13% and 31%, respectively. A woman with one first degree relative affected with ovarian cancer and one first degree relative affected with BC has an estimated risk of 40 percent of developing BC by age 79 years if the relative with BC was diagnosed in her thirties. Studies demonstrated the strength of the genetic association between breast and ovarian cancer in some families. These findings highlight the importance of considering a woman's family history of ovarian cancer in the calculation of her risk of BC [21]. Family history of ovarian cancer and BC in our study was 1.5% and 8.2%, respectively. History of BC has more affection toward ovarian cancer on detection of BC in a family but we can say that hereditary breast and ovarian cancer don't have strong effect on the incidence of breast cancer.

5. Conclusions

The mean age at diagnosis of BC in Iran is around 46 to 49 years. Tumor size in our study is lower than many studies. The organ as site of the most metastases was the lung in our patients, while in other studies it is the bone. There were much more triple negative patients in our study than in many other studies around the world.

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