Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2015; 3(8D):2980-2984 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2015.v03i08.046

Research Article

Epidemiology of breast cancer in young women in the West of Iran

Nasrin Amirifard, Mansour Choubsaz, Masoud Sadeghi*, Edris Sadeghi
Cancer Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran

***Corresponding author**
Masoud Sadeghi
Email: sadeghi_mbrc@yahoo.com

Abstract: The incidence of breast cancer (BC) in young women (age < 35) is low. The aim of the present study was to investigate clinico pathological characteristics in young BC patients (35 and less than 35 years old) for the first time in the West of Iran with focusing on recurrence. Between of 2001 to 2008, 79 women with BC referred to our Clinic that all patients had age≤35 years at diagnosis. Age, sex, stage, grade, survival, vascular invasion, perineural invasion, recurrence, tumor markers, lymph node invasion, history of BC, age at first menstruation and age at first pregnancy were checked in the patients. Estrogen receptor (ER) and progesterone receptor (PR) positivity was defined as≥10% positive tumor cells with nuclear staining. Nuclear grade I, II and III were for 25.3%, 49.4% and 25.3% patients and also 24%, 53.1% and 22.9% for histological grade I, II and III, respectively. Four patients (5.1%), 50(63.3%), 21(26.7%) and 3(3.9%) had stage I, II, III and IV, respectively. Out of 55 patients with lymph node invasion, 35 (63.6%) had 1-3 involvement lymph nodes, 17(30.9%) had 4-10 and 3(5.5%) had >10. Of all patients, 16(20.2%) had recurrence and 22 (27.8%) had history of BC. There was significant correlation between age, stage, metastatic lymph nodes and survival with recurrence (P<0.05). In conclusion, Low age, higher stage and lymph node metastases with four or more positive nodes are prognostic factors for recurrence in young patients with BC.
Keywords: Breast Cancer, Young age, Recurrence, Stage

INTRODUCTION

Breast cancer (BC) is a heterogeneous disease and is currently divided into subtypes in accordance with the status of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) [1]. A young age at diagnosis of breast cancer (BC) as a negative prognostic factor is a controversial issue [2]. The incidence of BC in young women (age < 35) is low. The biology of the disease in this age group is poorly understood, and there are conflicting data regarding the prognosis for these women compared to older patients [3]. Around 6.6% of all BC cases are diagnosed in women less than 40 of age, 2.4% in women less than 35, and 0.65% in women less than 30 [4,5]. The reports showed that young BC patients have more aggressive features, such as biologically more ER negative, higher histological grade, and more triple-negative subtype. Yet other studies have attributed the inferior outcome of young age to the more advanced presentation at diagnosis, including higher rates of axillary lymph node positivity and larger tumor size. Others have postulated that the effect of differential gene expression between different age groups might play a role [6]. Young women who receive breast-conserving therapy have a higher rate of local recurrence. Therefore, it is important to secure sufficient resection margins and consider boost radiotherapy to prevent local treatment failure. Special considerations regarding psychosocial factors and fertility should be taken into account for young patients [7].

The aim of the present study was to investigate clinico pathological characteristics in young BC patients (35 and less than 35 years old) for the first time in the West of Iran with focusing on recurrence.

PATIENTS AND METHODS

Between of 2001 to 2008 and in a retrospective study, 79 women with BC referred to our Clinic, Kermanshah city, Iran. All patients had age≤35 years at diagnosis. Age, sex, stage, grade, survival, vascular invasion, perineural invasion, recurrence, tumor markers, lymph node invasion, history of BC, age at first menstruation and age at first pregnancy were checked in the patients. Estrogen receptor (ER) and progesterone receptor (PR) positivity was defined as≥10% positive tumor cells with nuclear staining. The human epidermal growth factor receptor 2 (HER2) positive 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 [8]. The correlation between the variables was done by SPSS software v.19 (Chi-square test and T-test).

RESULTS

The mean age at diagnosis was 32.9 years (range, 20-35 years), 100% female. Twenty patients (25.3%), 39(49.4%) and 20(25.3%) had nuclear grade I, II and III and also 19 (24%), 42(53.1%) and 18(22.9%) for histological grade had grade I, II and III, respectively (Table 1). Four patients (5.1%), 50(63.3%), 21(26.7%) and 3(3.9%) had stage I, II, III and IV, respectively. Type of pathology for 76 patients (96.2%) was ductal carcinoma and for 3(3.8%) was lobular carcinoma. Fifty patients (63.3%), 47(59.5%) and 55(69.6%) had vascular, perineural and lymph node invasion, respectively. Out of 55 patients with lymph node invasion, 35 (63.6%) had 1-3 involvement lymph nodes, 17(30.9%) had 4-10 and 3(5.5%) had >10. HER2, ER and PR were positive for 40(50.6%), 58(73.4%) and 57(72.1%), respectively. Of all patients, 16(20.2%) had recurrence and 22 (27.8%) had history of BC.

Table 1: The characteristics for all patients with BC (n=79)

Variables	n(%)	Mean	Range
Age(year)		32.9	20-35
Sex			
Male	0(0)		
Female	100(100)		
Nuclear Grade			
I	20(25.3)		
II	39(49.4)		
III	20(25.3)		
Histological Grade			
I	19(24)		
II	42(53.1)		
III	18(22.9)		
Stage			
I	4(5.1)		
II	50(63.3)		
III	21(26.7)		
IV	3(3.9)		
Type of Pathology			
Ductal Carcinoma	76(96.2)		
Lobular Carcinoma	3(3.8)		
Vascular Invasion			
Yes	50(63.3)		
No	29(36.7)		
Perineural Invasion			
Yes	47(59.5)		
No	32(40.5)		
LN*Invasion			
Yes	55(69.6)		
No	24(30.4)		
Number of Invasive LN*(n=55)			
1-3	35(63.6)		
4-10	17(30.9)		
>10	3(5.5)		
HER2			
Positive	40(50.6)		
Negative	39(49.4)		
ER			
Positive	58(73.4)		
Negative	21(26.6)		
PR			
Positive	57(72.1)		
Negative	22(27.9)		
Recurrence			
Yes	16(20.2)		
No	63(79.8)		
History of breast cancer			
Yes	22(27.8)		
No	57(72.2)		

*LN: lymph Node

The prevalence of age at the first menarche and the first pregnancy has been shown in Table 2. There was no significant correlation between them with recurrence (P>0.05).

Table 2: The prevalence of age at the first menstruation and the first pregnancy for BC patients (n=79)

Variables	n(%)
Age at first menarche (year)	
11	7(8.9)
12	19(24.1)
13	22(27.8)
14	19(24.1)
15	12(15.2)
Age at first pregnancy(year)	
20	7(8.9)
21	4(5.1)
22	5(6.3)
23	10(12.6)
24	9(11.4)
25	13(16.4)
26	8(10.1)
27	3(3.8)
28	6(7.6)
30	5(6.3)
31	1(1.3)
32	4(5.1)
35	1(1.3)
No pregnancy	3(3.8)

Table 3 shows the correlation between recurrences with a number of variables in BC patients. There was significant correlation between these variables with recurrence (P<0.05), but there was no significant correlation between nuclear grade, histological grade, history of BC, HER2, ER, PR, type of pathology, vascular invasion and Perineural invasion with recurrence (P>0.05).

Table 3: The correlation between recurrence with a number of variables in BC patients (n=79)

Variables	Recurrence(positive) n=16	Recurrence(negative) n=63	P-value
Mean Age(year)	31.5	33.2	0.044*
Number of Invasive LN, n(%)			0.000**
0	1(4.2)	23(95.8)	
1-3	6(17.1)	29(82.9)	
4-10	6(35.3)	11(64.7)	
>10	3(100)	0(0)	
Stage, n(%)			0.000**
I	0(0)	4(100)	
II	4(8)	46(92)	
III	10(47.6)	11(52.4)	
IV	2(66.7)	1(33.3)	
Mean Survival (months)	39.2	58.3	0.000*

*T-test **Chi-square test

DISCUSSION

Young women with BC have a more unfavorable outcome and advanced disease than older women [9]. BC diagnosed in women 35 years of age or less accounts for <2% of all BC cases [10]. Diagnosis of BC in young patients (≤35) correlates with a worse prognosis compared to their older counterparts (>35) [6].

In a study, the clinicopathologic characteristics of 191 young female patients (under 40 years of age) diagnosed with breast carcinoma were studied that11 patients were stage 0, 21 stage I, 94 stage II, 38 stage III, 6 stage IV, and in 21 no information was obtained. Sixty five percent of patients had positive lymph nodes at diagnosis; 102 patients (54%) relapsed at a median of 29 months after diagnosis. Histologically, 180 cases were infiltrating BC, 150 ductal (83%), 19 lobular (11%) and 11 of special types (6%); 11 cases were ductal carcinoma in situ. There were no cases of medullary carcinoma. High nuclear grade and vascular invasions were frequent (68% and 67%, respectively) [11]. In other study, the characteristics for operable BCs in patients aged <40 years were positive lymph node (66.7%), histological grade (I,II and III were 2.4%, 48.8% and 48.8%, respectively), ER-positive (63%), PR-positive(51.1%), HER2-positive (74.4%), recurrence (7.9%) [2]. Of 187 cases of young BC patients less than 40 years, eighty-one cases had lymph node metastasis (43.3%), 126 cases had lymph vascular invasion (67.4%), and 125 cases had histological grade III (66.8%) disease, ER-positive (43.9%), PR-positive (35.3%), HER2-positive (35.8%), TMN stage (I, II and III were 20.3%, 63.1% and 16.6%, respectively) [12]. Of 669 cases of BC analyzed, 54 (8.1%) were in women 40 years old and younger. histological grade (I, II and III were 3.7%, 44.4% and 50%, respectively), Lymph vascular invasion (37%), ER-positive (96.3%), PR-positive (83.3%), TMN stage (I, II and III were 27.8%, 50% and 22.2%, respectively) [13]. Of 79 patients in our study, nuclear grade I, II and III were 25.3%, 49.4% and 25.3%, respectively and also histological grade 24%, 53.1% and 22.9% for grade I, II and III, respectively. 5.1%, 63.3%, 26.7% and 3.9% patients had stage I, II, III and IV, respectively. Type of pathology for 96.2% was ductal carcinoma and 3(3.8%) was lobular carcinoma. 63.3%, 59.5% and 69.6% had vascular, perineural and lymph node invasion, respectively. Out of 55 patients with lymph node invasion, 63.6% had 1-3 involvement lymph nodes, 30.9% had 4-10 and 5.5% had >10. HER2, ER and PR were positive for 50.6%, 73.4% and 72.1%, respectively. Of all patients, 20.2% had recurrence. Based on these results, percent of risk factors for young patients with BC in areas of world are different and to receive a good result, it needs a number of studies with emphasis on race and geographical location.

Many of the usual risk factors for BC in older women also increase risk in younger women including increasing age, Black race, family history, later age at first birth and menarche, radiation exposure and lack of physical activity [14]. One of the most important risk factors for local recurrence after breast-conserving surgery is age <35 years at presentation [4]. The recurrence rate was highest among women 45 years of age or younger at baseline [15]. Young age has been identified as a risk factor for recurrence and death from BC [15,16]. Other hypotheses to explain the remaining difference in survival between age groups after corrections for tumor characteristics are that the increased risk of local recurrence associated with low age, leads to an increased risk of BC death and that young women may differ from older with respect to the treatment they are given and their responsiveness to it, or presumably a combination of both [5]. Even with the use of chemotherapy, recurrence rates were significantly higher in the younger cohort due to the advanced stage at presentation [17]. It has been shown that patients with high grade tumors treated by mastectomy have significantly high frequency of lymph node metastases with four or more positive nodes; develop more systemic recurrences [18]. Furthermore, there is a direct relationship between the number of involved axillary nodes and the risk for distant recurrence [19, 20]. In our study, recurrence rates were significantly higher in low age, higher stage and lymph node metastases with four or more positive nodes. Also, the mean survival for the patients with recurrence was very low.

CONCLUSION

Low age, higher stage and lymph node metastases with four or more positive nodes are prognostic factors for recurrence in young patients with BC. To receive a good result about affection of risk factors for young patients, it needs a number of studies with emphasis on race and geographical location.

REFERENCES

1. Payandeh M, Malayeri R, Sadeghi M, Gholami F; Expression of p53 and Ki67 in the Patients with Triple Negative Breast Cancer and Invasive Ductal Carcinoma. American Journal of Cancer Prevention, 2015; 3(3):58-61.
2. Aryandono T, Harijadi, Soeripto; Breast cancer in young women: prognostic factors and clinico pathological features. Asian Pac J Cancer Prev, 2006; 7(3):451-4.
3. Han W, Kim SW, Park IA, Kang D, Kim SW, Youn YK, *et al.;* Young age: an independent risk factor for disease-free survival in women with operable breast cancer. BMC Cancer.2004; 4:82.
4. Anders CK, Johnson R, Litton J, Phillips M, Bleyer A; Breast cancer before age 40 years. Semin Oncol; 2009; 36(3):237-49.
5. Fredholm H, Eaker S, Frisell J; Breast cancer in young women: poor survival despite intensive treatment. PLoS One, 2009; 4(11):e7695.
6. Zhao Y, Dong X, Li R, Song J, Zhang D; Correlation Between Clinical-Pathologic Factors and Long-Term Follow-Up in Young Breast cancer Patients. Transl Oncol2015; 8(4):265-72.

7. Lee HB, Han W; Unique features of young age breast cancer and its management. J Breast Cancer, 2014; 17(4):301-7.
8. Payandeh M, Sadeghi M, Sadeghi E, Aeinfar M; Clinicopathology Figures and Long-term Effects of Tamoxifen Plus Radiation on Survival of Women with Invasive Ductal Carcinoma and Triple Negative Breast Cancer. Asian Pac J Cancer Prev, 2015; 16(12):4863-7.
9. Lee WY; Frequent loss of BRCA1 nuclear expression in young women with breast cancer: an immunohistochemical study from an area of low incidence but early onset. Appl Immunohistochem Mol Morpholm2002; 10(4):310-5.
10. Bayraktar S, Amendola L, Gutierrez-Barrera AM, Hashmi SS, Amos C, Gambello M, *et al.;* Clinicopathologic characteristics of BCin BRCA-carriers and non-carriers in women 35 years of age or less. Breast, 2014;23(6):770-4.
11. Bertheau P, Steinberg SM, Cowan K, Merino MJ; Breast cancer in young women: clinicopathologic correlation. Semin Diagn Pathol, 1999; 16(3):248-56.
12. Chen HL, Ding A, Wang FW; Prognostic effect analysis of molecular subtype on young BCpatients. Chin J Cancer Res, 2015; 27(4):428-36.
13. Lee MK, Varzi LA, Chung DU, Cao MA, Gornbein J, Apple SK, *et al.;* The Effect of Young Age in Hormone Receptor Positive Breast Cancer. Biomed Res Int, 2015; 2015:325715.
14. Yankaskas BC; Epidemiology of Breast cancer in young women. Breast Dis, 2005-2006; 23:3-8.
15. Cao JQ, Olson RA, Tyldesley SK; Comparison of recurrence and survival rates after breast-conserving therapy and mastectomy in young women with breast cancer. Curr Oncol, 2013; 20(6):e593-601.
16. Gajdos C, Tartter PI, Bleiweiss IJ, Bodian C, Brower ST; Stage 0 to stage III breast cancer in young women. J Am Coll Surg, 2000; 190(5):523-9.
17. Rudra S, Yu DS, Yu ES, Switchenko JM, Mister D, Torres MA; Locoregional and Distant Recurrence Patterns in Young versus Elderly Women Treated for Breast Cancer. Int J Breast Cancer, 2015; 2015:213123.
18. Hopton DS, Thorogood J, Clayden AD, MacKinnon D; Histological grading of breast cancer: significance of grade on recurrence and mortality. Eur J Surg Oncol, 1989; 15(1):25–31.
19. Saez RA, McGuire WL, Clark GM; Prognostic factors in breast cancer. Semin Surg Oncol, 1989; 5(2):102–110.
20. Nemoto T, Natarajan N, Bedwani R, Vana J, Murphy GP; Breast cancer in the medial half; results of the 1978 national survey of the American College of Surgeons. Cancer, 1983; 51(8):1333–38.