

RESEARCH COMMUNICATION

Breast Carcinoma in Young Women Aged 30 or Less in Northern Pakistan - the Armed Forces Institute of Pathology Experience

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Abstract

Objective: The study was carried out to document the occurrence of early onset breast cancer in our population and to assess prognostic variables. **Methods:** Records of a total of 1,644 female patients diagnosed with breast carcinoma during the last four years (Jan 2005 - Dec 2008) at the Histopathology Department, Armed Forces Institute of Pathology (AFIP) were retrieved from the AFIP tumour registry. All cases of breast carcinoma diagnosed in young females, 30 years of age or less, were selected and assessed for the type of specimen, tumour type, size and grade, presence or absence of lymph node metastasis, number of lymph nodes recovered and number of lymph nodes involved. Data were entered into SPSS version 11 to calculate mean, median, mode and standard deviation for quantitative variables and frequencies and percentages for qualitative variables. **Results:** The mean age was 28 ± 2.7 years and the mean tumour size was 3.7 ± 2.9 cm. Most frequent age group was 26-30 years (78.6%). The most common histological tumour type was invasive ductal carcinoma (88.7%), followed by invasive lobular carcinoma (5.4%). Seven out of 168 (4.2%) tumours were less than 2 cm in size, 69 (41.1%) were between 2-5 cm and 39 (23.2%) were greater than 5 cm. Grade 2 (57.1%), followed by grade 3 (29.8%) were the most frequent. Out of 68 cases in which lymph nodes were included, lymph node metastasis was seen in 55 (80.8%). **Conclusion:** Breast cancer is much commoner in young women in Pakistan as compared to the rest of the world. It is important to keep this in mind when evaluating even very young females with breast lumps.

Key Words: Breast carcinoma - young females - histopathology - tumour characteristics - Pakistan

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Introduction

Breast carcinoma is the leading cause of death in developed countries and one of the leading causes of death due to malignancies in developing countries like Pakistan (Siddiqui et al., 2008). Breast cancer is rare in young women especially in women less than 30 years of age. According to SEER data collected between 1975 and 2000, less than 1% of all breast cancer cases occurred in women under the age of 30. Breast cancer incidence rises steadily with age, stabilizes, and then drops slightly after 80 years of age (Brinton et al., 2008). There is an increase in incidence of breast cancer with increasing age, from an average incidence per million of 1.3 in 15- to 19-year-olds, to 12.1 in 20- to 24-year-olds, to 81.1 in 25- to 29-year-olds (Hall et al., 2005; Jatoi et al., 2005).

Breast cancer in young women deserves special consideration because of the complex issues associated with it. It may present differently from breast cancer in older women and may be more difficult to diagnose (Kriuchkov and Freund, 2007). There are special considerations of pregnancy, fertility and contraception,

sexuality and body image (Pagani et al., 1998). Variables of prognostic significance are tumour size, type, grade, lymph node status, skin involvement and receptor status. Tumours tend to be larger (median tumour size 2 cm in young women vs. 1.5 cm in older women), more advanced at diagnosis (more likely to be lymph node positive) and more aggressive (less well differentiated) than breast cancer in older women (Okugawa et al., 2005). Cancer in young women also has a higher mortality and shorter disease free survival than in older women, and is more likely to recur after treatment both locally and at distant sites (El Saghir et al., 2006).

There are several challenges in the diagnosis of breast cancer in young women. Mammography has much lower accuracy in young women, mostly due to the greater tissue density in younger women which may obscure lesions, and partly because some breast cancers in this group do not have typical malignant features on mammography (Duffy et al., 2006). Ultrasound has been found more accurate than mammography in younger women and is considered the imaging test of choice. The addition of percutaneous biopsy (fine needle aspiration biopsy

[FNAB] or core biopsy) to the clinical evaluation and imaging findings increases the chances of correctly diagnosing a malignant lesion (Kocjan et al., 2008). According to SEER analysis, five-year survival rates for breast cancer, by age, revealed that survival was lowest for those in the adolescent and young adult age group. Within that group, 25- to 29-years old women had slightly lower survival rates than those younger or older (Horner et al., 2009).

In the recent past we have realized that in Pakistan also, more and more young females are being diagnosed to have breast carcinoma. We have also noted that breast carcinomas in young patients are aggressive with bigger tumour size, more lymph nodes involvement and higher grades. The objective of this study was to document the increased occurrence of early onset breast cancer in our population and to assess the prognostic variables in our patients.

Materials and Methods

Record of a total of 1644 female patients diagnosed to have breast carcinoma during the last four years (Jan 2005 – Dec 2008) at Histopathology department, Armed Forces Institute of Pathology (AFIP) was retrieved from AFIP tumour registry. From this record all cases of breast carcinoma diagnosed in young females, 30 years of age or less were selected. These cases were assessed for type of specimen, tumour type, tumour size, tumour grade, presence or absence of lymph node metastasis, number of lymph nodes recovered and number of lymph nodes involved. Data was entered in SPSS version 11. Mean, median, mode and standard deviation were calculated for quantitative variables like age, tumour size, tumour grade and number of lymph nodes involved. Frequencies and percentages were calculated for qualitative variables like tumour type and presence or absence of lymph node metastasis.

Results

Out of a total of 1644 patients diagnosed as breast carcinoma 168 (10.2%) patients were 30 or less than 30 years of age. The ages ranged from 16 to 30 years with mean age of 28+2.7 years. The tumour size ranged from 0.5cm to 13 cm with mean size of 3.7+2.9 cm. Number of involved lymph nodes ranged from 4 to 32 with a mean of 4+5.5. Most frequent age group was 26-30 years (78.6%), followed by 21-25 years (19.6%) and then 16-20 years (1.8%). There were no patients less than 16 years of age.

Out of total of 168 specimens, 88(52.4%) were mastectomies, 42(25%) were lumpectomies and 38(22.6%) were biopsies. The most common histological tumour type was invasive ductal carcinoma (88.7%), followed by invasive lobular carcinoma (5.4%), mixed invasive ductal and lobular carcinoma (3%) and few each of other types including medullary, mucinous, pleomorphic and metaplastic carcinomas (3%)(Table2). Seven out of 168 (4.2%) tumours were less than 2 cm in size, 69(41.1%) were between 2-5 cm and 39 (23.2%)

Table1. Association of Age Group with Tumour Characteristics

Variables	Age group(yrs)	16-20	21-25	26-30
Specimen type	Mastectomy	2	15	71
	Lumpectomy	0	10	32
	Trucut biopsy	1	8	29
Tumour type	Ductal	2	28	119
	Lobular	1	1	7
	Mixed	0	2	3
	Other	0	2	3
Tumour size(cm)	<2	0	1	6
	2-5	1	15	53
	>5	0	7	32
	Not assessable	2	10	41
Tumour grade	GradeI	0	1	5
	GradeII	1	17	78
	GradeIII	1	12	37
	Not assessable	1	3	12
Metastasis	Present	0	11	3
	Absent	0	1	21
	Not assessable	3	21	76
Positive lymph nodes	0	0	1	12
	1-3	0	4	4
	4-9	0	3	24
	10 and more	0	4	16
	Missing	3	21	76

Table 2. Frequencies of Tumor Types

Tumour type	Number
Invasive ductal carcinoma	149
Invasive lobular carcinoma	9
Mixed invasive ductal and lobular carcinoma	5
Pleomorphic carcinoma	2
Medullary carcinoma	1
Mucinous carcinoma	1
Metaplastic carcinoma	1

were greater than 5 cm. Tumour size could not be determined in 53 cases as 38 cases were biopsies and in the remaining 15 cases only blocks and slides were received for review and receptor studies.

The most frequent tumour grade was grade 2 (57.1%), followed by grade 3 (29.8%) and grade 1 (3.6%). Grade could not be assessed in 16(9.5%) of cases as the tissue was scanty or showed extensive autolysis. The lymph node status could not be determined in 100 cases as these cases included trucut biopsies, lumpectomies and simple mastectomies. Out of 68 cases in which lymph nodes were included, lymph node metastasis was seen in 55(80.8%) of cases. Thirteen patients had no lymph node involvement, 8 patients had metastasis in 1-3 lymph nodes, 27 in 4-9 lymph nodes and 20 cases showed ten or more than ten lymph nodes involved.

Discussion

Breast carcinoma is one of the leading causes of death all over the world. Prognosis of breast carcinoma has been associated with many variables for example age, tumour size, tumour grade, histological type, lymph node status, receptor status etc. All the above mentioned variables have got prognostic significance but age has been repeatedly

proved to be one of the most important prognostic factors which has effect on five year survival rates and also mortality and disease free survival rates (Hall et al., 2005; Jatoi et al., 2005; Brinton et al., 2008; Siddiqui et al., 2008). Many studies have been conducted to study the prognostic variables in young females having breast carcinomas. The cutoff age limit to designate the patient as young has also been different. In some studies young females have been described as those less than 40 years of age and in less than 35 years. We designated a cutoff point of 30 years for our study considering the increasing recent trend in our population of women being diagnosed as breast carcinoma at 30 or less than 30 years of age.

According to SEER less than 1% of breast carcinoma occurred in women less than 30 years of age (Horner et al., 2009). The highest incidence rate and mortality rate of breast carcinoma in young females is in African Americans followed in descending order by Hispanics, American Indians, White Non Hispanics and Asians (Horner et al., 2009). According to Anyanwu (2008) about 8% of females of 30 and less than 30 years of age are diagnosed to have breast carcinoma in third world countries. In a study by Tabbane et al (1985) 3.8% of breast carcinoma was diagnosed in females less than 30 years of age. In two different Australian studies the percentages of breast carcinoma in young female were 2% and 6% respectively but their cut off inclusion criteria for young women were 35 years and 40 years, respectively (Brennan et al., 2005; Hickey et al., 2009). A study from UK reported that breast carcinoma diagnosed in women less than 35 years of age constituted 2% of the total cases (Pharoah et al., 2000). A Danish study showed a percentage of 8.3% in which cut off value for young age of taken as 35 years (Kroman et al., 2002).

An earlier Pakistani study has reported 18% tumours occurring in women less than 35 years age (Siddiqui et al., 2008). In our study we found 10.2% occurring in young women which is very high considering a very low cutoff age limit of 30 years. In two previous studies on breast carcinoma also conducted at Histopathology department of Armed Forces Institute of Pathology, Rawalpindi in 1980 and 1996, the percentage of breast carcinoma in women of 30 or less than 30 years of age was 10% each (Malik et al., 1994; Rashid et al., 1996).

Tumour size is one of the strongest prognostic indicators even after 20 years of follow-up. Generally tumour size in younger patients is larger. In our study 58.2% tumours had size between 2-5 cm and 35.2% greater than 5cm. In the local study by Siddiqui et al (2008) only 25% had tumour size < 2cm while in the current study only 4.2% of tumours were of this category. In study by Kroman et al (2002) 38.1% and 8% of patients less than 35 years had tumour sizes in the range of >2-5 cm and >5 cm respectively. In study by Jimor et al (2002) 40% and 25% of patients less than 35 years of ages had tumour sizes in the range of >2-5cm and >5cm respectively. In study by Saleh ad Abdeed (2007) 53.6% tumours were between the range of 2-5cm and 31.3% greater than 5cm. Okugawa et al (2005) study depicted 48% of the tumours in the range of 2-5 cm. Kothari et al (2002) studied 12 patients under the age of 25 years, and

found that 7 patients had tumour size less than 2 cm, 3 patients >2-5 cm and 2 greater 5cm. Thus majority of the studies show most patients presenting with tumour size greater than 2cm.

In our study increasing tumour size was associated with increased rate of lymph node metastasis. Out of 60 patients in which the tumour size was greater than 2 cm (26 cases 2-5 and 24 greater than 5cm) lymph node metastasis was found in 50 cases (83%). In the study by Kurumiya et al (2002) the prevalence of lymph node metastasis was higher as the tumor enlarged. There was significant correlation between the size of the primary breast tumor and lymph node metastasis ($p < 0.0001$). Study of Nouh et al (2004) revealed that 62% of T1 tumors metastasize to greater than 3 lymph nodes in contrast to 74.3% of T3 tumors.

The prognostic value of histological type varies a lot. Breast carcinoma types with an excellent prognosis, such as invasive cribriform, tubular, tubulo-lobular and mucinous show >80% survival at 10 years. Tubular mixed, mixed ductal with special type, atypical medullary and alveolar lobular carcinoma have a good prognosis with a 60-80% 10-year survival. Those with invasive papillary, classic lobular and medullary cancers have a worse prognosis. Finally, 10-year survival among those with ductal, solid lobular, mixed ductal and lobular carcinoma is below 50%. In most populations infiltrating ductal carcinoma constitute about 70% of all diagnoses. In studies by Saleh and Abdeen (2007) and Okugawa et al (2005) invasive ductal carcinoma constituted 93% and 83.1% of invasive ductal carcinomas respectively. In our study also the most common histological tumour type was invasive ductal carcinoma (88.7%), followed by invasive lobular carcinoma (5.4%).

The most widely used grading systems is the Scarff-Bloom-Richardson classification. The validity of grading has been subjected to inter-observer reproducibility and subjectivity However higher grades have been quite consistently associated with lower long-term survival. In our study the most frequent tumour grade were Grade 2 (57.1%), followed by Grade 3 (29.8%) and Grade 1 (3.6%). Other studies of early onset breast cancer show more of Grade 2 and Grade 3 tumours. In study of Kroman et al 15 combined percentage of Grade 2 and 3 tumours was 63%. Kothari's study revealed a percentage of 63% for Grade 3 tumours. In study by Jimor et al 81% and 19% of tumours were Grade 3 and 2 respectively. Likewise Okugawa reported percentages of Grade 1, 2 and 3 tumours respectively as 24%, 53% and 23% and Saleh et al study reported these percentages as 10.2%, 50.6% and 23%.

Lymph node involvement is a valuable indicator of long-term survival. In Okugawa's study 54% of the patients had no lymph node metastasis, 21% had metastasis in range of 1-3 lymph nodes and 25% had more than three involved lymph nodes. In our study 40% of patients had metastasis in more than three lymph nodes. Node- positive patients have about a 4-8 times higher mortality than those without nodal involvement. Patients with 10 or more involved axillary nodes showed 70% more deaths at 10 years than for those with 1-3 involved

nodes .

In conclusion, breast cancer is much commoner in young women in Pakistan as compared to the rest of the world . It is important to keep this in mind when evaluating even very young females with breast lumps .

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