

Correlation between the size of the breast lump and axillary lymph node metastasis in patients with carcinoma of breast.

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ABSTRACT

Background: Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in females, accounting for 23 percent of total cancer cases and 14 percent of cancer deaths.¹ The lifetime probability of developing breast cancer is one in six overall (one in eight for invasive disease).² In Bangladesh breast cancer is the 2nd most common cancer and also 2nd most leading cause of cancer death among the female population after cervical cancer.³ Despite the decreases in incidence rates in North America, breast cancer incidence has been increasing in other parts of the world, such as Asia and Africa. These international differences are thought to be related to societal changes occurring during industrialization.^{4,5}

Methods: This was a Prospective Observational cross-sectional study conducted among the 150 adult patients of breast carcinoma admitted in Department of surgery of Dhaka Medical College & Hospital, Bangabandhu Sheikh Mujib Medical University and Ahsania Mission Cancer & General Hospital during July 2012 to June 2013. After admission in surgery department, diagnosed patients (by ultrasonography and FNAC) with breast cancer were evaluated by history and physical examination, ultrasonography or mammography in a data collection sheet by the study physician. Tumor size was measured by physical examination, ultrasonography or mammography and during histopathological slide preparation. Histopathology of the dissected axillary lymph nodes determined the axillary lymph node status. Case record forms with appropriate questionnaire were filled for all patients.

Results: This prospective documented study enrolled 150 cases of diagnosed breast cancer patient. The mean (\pm SD) age of the patients was 42.16 ± 11.18 years with the range from 18 – 65 years. In this study, commonest presentation was painless breast lump in case of 84% patients. Next to it was nipple retraction (40%). Clinically, 52% of study populations were at stage II. Histologically, most of the tumor was at T₂ stage (2.1 to 5 cm). Duct cell carcinoma was the predominant histological type (99.33%) and 58% patient had grade II tumors. 66% population showed metastasis of tumor cells in the axillary lymph node(s). Frequency of axillary lymph node metastasis increased as the tumor size increased. We found 33.33% T1 tumors had axillary lymph node metastasis, where as 58.97% T2 tumors and 93.75% T3 tumors showed axillary lymph node metastasis respectively.

Key words: Carcinoma, Carcinoma of breast, Axillary lymph nodes.

Introduction

Breast cancer incidence rates were highest in North America, Australia/New Zealand, and in western and northern Europe and lowest in Asia and sub-Saharan Africa.^{1,6} Despite the decreases in incidence rates in North America, breast cancer incidence has been increasing in other parts of the world, such as Asia

and Africa. These international differences are thought to be related to societal changes occurring during industrialization (e.g. changes in fat intake, body weight, age at menarche, and/or lactation, and reproductive patterns such as fewer pregnancies and later age at first birth).^{4,5} In the early 1980s, breast

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cancer rates rose steeply by 3.7 percent per year over the baseline incidence which was most likely the result of increasing use of screening mammography. After increasing from 1994 to 1999, breast cancer incidence rates decreased from 1999 to 2007 by 1.8 percent per year.² Potential contributory factors to this decline include discontinuation of Hormone Therapy.

The presenting complaint in about 70% of patients with breast cancer is a lump (usually painless, 20% as a painful lump) in breast. About 90% of breast masses are discovered by the patient herself. Less frequently; 10% of patients present with nipple change(erosion, retraction, enlargement or itching of the nipple), 3% of patients present with nipple discharge, 5% of patients present with skin contour changes, redness, generalized hardness, enlargement or shrinking of the breast⁷. An initial physical examination can distinguish a cancerous breast lesion on the basis of some classic characteristics like single lesion, hard in consistency, irregular border, fixity with surrounding structures and palpable regional lymph node. In any patient who presents with a breast lump or other symptoms suspicious of carcinoma, the diagnosis should be made by a combination of clinical assessment, radiological imaging and a tissue sample taken for either cytology or histopathological analysis, the so called triple assessment.⁸ Once a diagnosis of breast cancer is established, it is important to accurately define the initial extent of disease (stage of tumor) since breast cancer stage affects subsequent treatment decisions. □ Breast cancer is classified according to the American Joint Committee on Cancer and the International Union for Cancer Control (AJCC-UICC) TNM breast cancer staging system⁹.

Tumor size has long been recognized as an independent prognostic factor and as a predictor of axillary node status, with larger tumors being associated with a worse prognosis and an increased likelihood of nodal metastasis. The most significant prognostic factor in breast cancer is the presence or absence of axillary lymph node involvement which is usually assessed at the time of surgery using sentinel lymph node biopsy or axillary lymph node dissection. Macro metastases (>0.2 cm in size) have clearly been shown to have prognostic significance.¹⁰

Method and Material:

This was a Prospective Observational cross-sectional study conducted among the 150 adult female patients with breast carcinoma admitted in Department of surgery, Dhaka Medical College & Hospital and Bangabandhu Sheikh Mujib Medical University during July 2012 to June 2013. After reporting in surgery department, patients with breast lump were evaluated by history and physical examination by the study physician. Diagnosis was made by ultrasonography or mammography and confirmed by FNAC. Tumor size was measured by physical examination, ultrasonography or mammography and during histopathological slide preparation. Histopathology of the dissected axillary lymph nodes determined the axillary lymph node status. Informed written consent was obtained from the patient's attendant after full explanation of the disease process. Evaluation was made by history and physical examination in a structured case record form (CRF) by the study physician. Qualitative data were presented as frequency and percentage and Quantitative variable presented as mean and standard deviation. All data were processed and analyzed manually and by SPSS (Statistical Package for Social Science) 16 windows version.

Results:

This prospective documented study enrolled 150 cases of diagnosed breast cancer patient. The mean (\pm SD) age of the patients was 42.16 ± 11.18 years with the range from 18 – 65 years. In this study, commonest presentation was painless breast lump in case of 84% patients. Next to it was nipple retraction (40%). Clinically, 52% of study populations were at stage II. Histologically, most of the tumor was at T2 stage (2.1 to 5 cm). Duct cell carcinoma was the predominant histological type (99.33%) and 58% patient had grade II tumors. 66% population showed metastasis of tumor cells in the axillary lymph node(s). Frequency of axillary lymph node metastasis increased as the tumor size increased. We found 33.33% T1 tumors had axillary lymph node metastasis, whereas 58.97% T2 tumors and 93.75% T3 tumors showed axillary lymph node metastasis respectively.

Table I: Age distribution of the study patients (n=150).

Age group (years)	No. of Cases	Percentage
10 – 20	12	8%
21 – 30	12	8%
31 – 40	45	30%
41 – 50	57	38%
51 – 60	15	10%
61 – 70	9	6%
Mean \pm SD	42.16 \pm 11.48	
Median	42.50	
Range (min - max)	(18-65)	

Table II: Distribution of study population according to clinical symptomatology (n = 150)

Clinical Presentations	No. of Cases	Percentage
1.Painless breast lump	126	84%
2. Painful Breast lump	24	16%
3. Nipple discharge	12	8%
4. Nipple retraction	60	40%
5. Skin ulceration	6	4%
6. Lump in axilla	21	14%
7.Recent bone pain	3	2%
8. Recent cough	3	2%
9. Weight loss	10	6.67%

Table III: Distribution of study population according to clinical stage of the disease. (n = 150)

Stage	No. of Cases	Percentage
I	18	12.00%
II	78	52.00%
III	54	36%

Table IV: Histological characteristics of the tumor in study population (n=150)

Character	Findings	No. of Patients	Percentage
1. Size	Up to 2 cm	24	16%
	2.1 to 5 cm	78	52%
	> 5 cm	48	32%
2. Focality	Unifocal	148	98.67%
	Multi-centric	2	1.33%
3.Histological type of tumor	Infiltrating duct cell carcinoma	146	97.33%
	Others	4	2.67%
	Grade I	21	14%
4. Histological grading	Grade II	87	58%
	Grade III	42	28%
	Grade I	21	14%
5. Lympho Vascular Invasion	Present	29	19.33%
	Absent	121	80.67%

Table V: Distribution of study population according to lymph node involvement (Histopathological) (n=150)

Character of lymph node	Findings	No. of Patients	Frequency Percentage
1.Lymph node involvement	Involved	99	66.00%
	Not involved	51	34.00%
2.Number	1 to 3	70	46.67%
	4 or more	29	19.33%

Table VI: Distribution of study population according to lymph node involvement in relation to size (Histological). (n=150)

Size	No. of Patients (n)	Involvement of Lymph Node Findings	No. of Patients	Percentage	P Value
1. up to 2cm (T ₁)	24	Involved	8	33.33%	0.034
		Not involved	16	66.67%	
2. 2.1 cm to 5cm (T ₂)	78	Involved	46	58.97%	
		Not involved	32	41.02%	
3. > 5 cm (T ₃)	48	Involved	45	93.75%	
		Not involved	3	6.25%	

P Value based on Chi-Square test.

P Value < 0.05 is statistically significant.

Discussion:

Breast cancer is the most frequently diagnosed cancer among women and the leading cause of cancer death in females worldwide. In Bangladesh breast cancer is the 2nd most common cancer and also 2nd most leading cause of cancer death among the female population after cervical cancer³. Because of high incidence rate of breast cancer among women, it is essential to identify effective strategies to manage this disease in populations. This is particularly depended on screening programs and early detection of cancer, information about risk factors, incidence of cancer in a population and the relationship between tumor characteristics and its invasive manner.

In our study most of the patient was encountered in 41 – 50 years (38%) age group and the mean (\pm SD) age was 42.16 ± 11.48 years with ranged from 18 to 65 years and majority was older than 40 years. A study of 380 patients in Singapore, done by LGL Tan et al. showed the median age of the subject was 52 years with the range from 24 – 87 years¹¹. Indian author Amrut V. et al found the mean age of patient at the time of surgery was 49.32 years which ranged from 26 – 80 years and 51 (53.68%) patient was below 50 years of age in their study¹². Elahe Orang et al. done their study in Iran where they found mean age of the participants was 48.93 ± 12.6 years (ranged from 18 – 90 years)¹³. Another study conducted in Lady Reading Hospital; Pakistan by Muhammad Naeem et al. showed breast cancer was most common in the 40 – 49 years age group (30.4%)¹⁴. It is not yet clear that whether this high young onset is due to adaption of a more westernized life style and diet or due to intense environmental exposure.

Symptomatology analysis of the study population reveals that breast lump (n= 150) is the commonest presentation of which painless and lump predominates (n= 126). In this study after breast lump the commonest presentation was nipple retraction 40% (n= 60) and Paget's disease of the nipple was associated in 3 case. In other parts of world around 10% patient presents with nipple retraction. In our country the incidence is more as because we get patients in advance stage. About 14%

patients had associated lump in axilla and 8% had nipple discharge. Different study revealed 5 -12% breast cancer patient complaints of nipple discharge during presentation.¹⁵ A few study populations presented with skin ulceration (4%), weight loss (6.67%) and signs of metastasis (2%).

Clinical stages in which disease presented included 18 cases (12%) of stage I, 78 cases (52%) of stage II & 54 cases (36%) of stage III disease. This data projects that we are getting early breast cancer cases as well as late cases in relatively same quantity. Many other international studies conducted in USA, Malaysia, Germany and India has shown that breast cancer is detected more commonly in much earlier stage (0, I, II) due to better screening program^{16,17,18}, whereas majority of studies conducted in Pakistan shows that they get breast cancer cases in mostly at stage III & IV¹⁴. Variation in the incidence of breast cancer among multicultural population suggests different etiological factors including genetics, environment, reproductive experience, endogenous & exogenous hormones, immune status, host vulnerability, cultural dynamics, socio-demographic differences and behavioral characteristics across populations¹⁹.

We assessed following variables in the histological characteristics of the tumor – histologic type, tumor size, focality, histological grading and lymphovascular invasion. Expectedly invasive duct cell carcinoma was the most common histologic type (97.33%) which is comparable with other studies done by Hunter CP (2000), Kuraparthi S. et al. (2007), LGL Tan et al. (2005), Amrut V. et al. (2011), Elahe Orang et al. (2013). In this study we have observed T2 tumors in highest number (52%) followed by T3 tumors (32%) and a little T1 tumors (16%). Various studies done in India, Korea, USA, Iran, Malaysia by different researchers shows that they also receive majority cases in T2 stage followed by T1 stage. They used to get a very little number of T3 tumors^{12, 13, 20, 21}. This may be due to lack of awareness in rural areas about breast cancer & to a certain extent due to failure of development of national breast screening program in our country.

A common route of spreading of breast carcinoma is first through the axillary lymph nodes²². In our study we found 66% patients had positive axillary lymph

nodes and among them majority had 1-3 positive lymph node (46.67%) and rest had 4 or more positive lymph nodes. Certain other researches have also obtained similar result^{12,23}.

Various studies have accepted that breast carcinoma spreads first through the auxiliary lymph node and the incidents of axillary lymph node involvement increases with larger tumors (Silverstein)²². In our study we have investigated whether there is any relationship between tumor size and its invasive manner in the form of ALNM (axillary lymph node metastasis). According to tumor size we have divided the study population into main 3 groups (T₁, T₂, T₃). Our result demonstrates the strong relationship between primary tumor size and ALNM. As the tumor size increased the frequency of positive axillary lymph nodes also increased. As shown in table VI, T₃ tumor size (more than 5 cm) had higher ALNM compared to other groups. Our result is comparable with others studies (Elahe O, Silverstein, LGL Tan) and also confirmed by Chi-Square test to be statistically significant.

ALNM is the most important prognostic factor for operable breast carcinoma and can be predicted by several factors. In different countries several researchers have done various studies on these predictors of ALNM and most of them have found tumor size as an important and independent predictor. Now-a-days it is given emphasis on predicting ALNM pre-operatively as because many of the predictors can be determined pre-operatively by imaging and true cut biopsy. Moreover there is ongoing invention of newer reliable techniques for axillary staging – SLNB(sentinel lymph node biopsy), Lymphatic mapping etc.

Conclusion:

The presence or absence of ALNM remains the most important prognostic factor in patients with potentially curable carcinoma of the breast and the development of effective adjuvant systemic therapies has made recognition of these metastasis critical for patient's management. This cross-sectional observational study was done on 150 carcinoma breast diagnosed patients who underwent simple mastectomy with ALND. According to histopathological study 66% of

study population showed ALNM. In relation to size 1/3 of T₁ tumors showed ALNM. Whereas 1/2 of T₂ tumors and almost all T₃ tumors involved axillary lymph node. So, tumor size is an important predictive factor for axillary lymph node metastasis.

Conflict of interest: None.

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