

Breast carcinoma over three decades in northern Pakistan — are we getting anywhere?

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Abstract

Objective: To compare the histological prognostic markers in breast carcinoma over three decades in Northern Pakistani population and analyse for any change in trends in terms of prognostic markers.

Methods: Cross-sectional descriptive study was carried out from January 2004 to December 2006 at AFIP, Rawalpindi on 822 cases of female breast carcinoma. Assessment of tumour size on gross examination followed by microscopic evaluation of tumour type, tumour grade, lymph node metastasis and skin involvement was done. The results of the present data were compared with studies of Wahid et al (January 1994 to December 1997) and Malik et al (January 1984 to December 1986) from the same institute.

Results: Total 822 cases of breast cancer were diagnosed with 541(64.9%) cases of mastectomy. The mean age was 48 ± 12 years with a mean tumour size of 4.6 ± 2 cm. A tumour size of >5 cm was seen in 30.6% cases and only 18.8% cases had a size <2 cm. Infiltrating ductal carcinoma was the commonest subtype in 674 (81%) cases with histological grade II in 533(64%) cases. Lymph node metastasis was present in 74.6% cases and skin involvement in 36% cases. The comparison of the results of the present study with those over the past two decades in Pakistan show that the mean age at diagnosis remains around 48 years. There is statistically significant increase in the tumours of <5 cm at presentation and a higher frequency of tumours with dermal invasion. No significant change is seen in frequency of lymph node metastasis at operation and tumour grade.

Conclusion: The comparison of results of other studies done over the past three decades in the region are not very encouraging. The age of presentation remains younger as compared to the West. A positive note is seen in terms of a decreasing tumour size but lack of DCIS cases in our material underlines the need of mammography and launching of effective screening programmes at the national level. Early detection of cases will help in treatment and subsequently improve prognosis in these patients as advocated by the West (JPMA 59:835; 2009).

Introduction

Breast cancer is the commonest carcinoma in women.¹ It accounts for 22% of all female cancers worldwide and approximately 42% cases occur in the developing countries.¹ High risk areas are North America, Europe and Australia. Prognosis and management of breast cancer are influenced by classic variables such as histological type, tumour grade, tumour size, lymph node status, hormone receptor expression along with Her-2/neu status.^{2,3} Carcinoma breast is also the commonest cancer of females in Southern and Northern Pakistan according to the Karachi tumour registry and AFIP tumour registry.^{4,5} Data for the last decade from AFIP tumour registry⁵ showed 26% of all malignancies to be breast cancer which also accounted for 42% of the total malignancies treated at Shaukat Khanum Memorial Cancer Hospital over the past ten years.⁶

Advanced stage of presentation has remained a dilemma for the treating oncologists and surgeons in our country. Many NGOs, hospitals and clinics have been running programmes to increase awareness about this malignancy but currently there is no national population

based screening programme.

The objectives of this study were to compare the histological prognostic markers in breast carcinoma from the same population over three decades and to analyse for any observable change in these parameters. The period from 2004 to 2006 was considered as representative of the current decade and these findings were compared with similar published studies at the same institute carried out from 1984 to 1986 and 1994 to 1997 in the same department to see the trend over the past two decades. A similar model has been adopted in a Danish study as well to see the effect of time trends on stage at presentation.⁷

Materials & Methods

This study was carried out at Histopathology department, Armed Forces Institute of Pathology (AFIP), Rawalpindi. AFIP is a tertiary care referral laboratory with samples from military hospitals and as well as civil public and private sector hospitals from upper Punjab, NWFP and adjacent Rawalpindi Islamabad region. All the cases of breast carcinoma diagnosed during January 2004 to December 2006

were included in the study. Gross measurement of the tumour size followed by confirmation by microscopy was done in cases of lumpectomy and mastectomy. Formalin fixation followed by paraffin embedding of the specimen was used with haematoxylin and eosin staining of the slide sections for subsequent microscopy. Histological type of the tumour, lymph node metastasis and skin involvement was assessed on routine H&E sections. Histological tumour grading was done using Modified Bloom Richardson scoring system.⁸ The results of the present data were compared with those of similar studies by Wahid et al⁹ and Malik et al¹⁰ from the same institute including the same population. The study by Malik et al included mastectomy specimens received between January 1984 and December 1986 whereas Wahid et al included all mastectomy specimens received between January 1994 and December 1997.

All the results were entered into the SPSS version 15 and analysed statistically. Frequency and means of the descriptive variables like age and prognostic markers were calculated. The frequency and means of this study were compared with earlier studies of Wahid et al⁹ and Malik et al¹⁰ using proportion test and taking a p-value of <0.05 as significant. All the values were two tailed.

Results

During the study period from January 2004 to December 2006 a total 822 cases of breast cancer were diagnosed. There were 541 (64.9%) cases of mastectomy, 167 (12.5%) cases of lumpectomy and 114 (13.7%) cases of trucut,

Age in years

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Figure: Frequency distribution of breast carcinoma in different age groups (n=788).

wedge or incisional biopsy. The mean age was 48 ± 12 years and the highest number of cases was seen in the fifth decade (Figure).

Mean tumour size was 4.6 ± 2 cm with a range of 0.5-20cm. This was assessed in 638 cases as it could not be adjudged in cases of incisional, trucut or wedge biopsy. A tumour size of >5cm was seen in 30.6% cases while 18.8% cases had a size <2 cm.

Infiltrating ductal carcinoma was the commonest subtype with 674 (81%) cases. While 58 (7%) cases were infiltrating lobular carcinoma. Maximum cases were of histological grade II consisting of 533 (64%) cases followed by 256 (30.7%) cases of grade III and 44 (5.3%) grade I tumours.

Table: Comparison of prognostic markers in female breast carcinoma over three decades.

Prognostic parameter		Malik et al 1984-1986 (n=280) %	Wahid et al 1994-1997 (n=100) %	Present study 2004-06 (n=833) %	p=value 1984-86 & 2004-06	p=value 1994-97 & 2004-2006
Histological type	Infiltrating ductal carcinoma	93	98	80.8	0.0036	0.0034
	Infiltrating lobular carcinoma	3	<1	6.1		
	Others	4	1	13		
Histological grade	Grade I	6	1.5	5.3	0.330	<0.0001
	Grade II	61	36.5	64		
	Grade III	33	62	30.7		
Tumour size	<2cm	-	8	18.8	<0.0001	0.0045
	2.1-5cm	-	44	50.5		
	>5cm	61	48	30.6		
	<5cm	32	52	69.4		
Lymph node metastasis	Present	79	74	74.6	0.202	0.92
	Absent	21	26	25.4		
Lymph nodes with metastasis	1-3	29	70	35.6		
	>4	71	30	64.2		
	4-6	30	-	16.4		
	>6	41	-	47.9		
Age range in years	20-76	23-73	16-100			
Age	5th decade	36	34	27.9		
	4th decade	-	29	21.5		
	3rd decade	2	10	8.5		
Skin involvement	Present	22	21	36.2	0.01	0.0094
	Absent	78	79	63.8		

Lymph node metastasis was present in 74.6% cases at the time of mastectomy. 35.6% cases showed up to 3 lymph nodes involved by the tumour whereas 47.9% cases showed more than six lymph nodes involved. Maximum 39 lymph nodes were recovered from any single case with axillary clearance and highest number of lymph nodes involved in a case was 35. Skin involvement in the form of dermal invasion or Paget's disease was seen in 36% cases.

Table shows the summary of the clinicopathological features of the present study in comparison with Wahid et al⁹ and Malik et al¹⁰ carried out at the same institute. There is statistically significant increase in the tumours of <5cm and <2cm at presentation and a higher frequency of tumours with dermal invasion. No significant change was seen in frequency of lymph node metastasis at operation or tumour grade.

Discussion

Carcinoma breast continues to be the commonest malignancy in pre and postmenopausal women in Pakistan. The late presentation and advanced stage of disease in Pakistani women have been attributed to poor literacy, conservative society and absence of screening programmes.⁸ It is interesting to note that other Asian countries like India, Japan, China and Philippines have a much less incidence of breast cancer as compared to Pakistan even though prevalence of the risk factors is similar.^{11,12}

The comparison of the results of the present study with those over the past two decades in Pakistan show that the average age at diagnosis remains around 48 years. There is an equal proportion of female patients with age less than 40 years, in the fifth decade and of age more than 50 years. However Wahid et al showed 58% cases in the postmenopausal group.⁹ Therefore younger ages at presentation persists in female breast cancer in Pakistan as compared to the West where the median age of presentation is 61 years^{8,13} as also reported in other local studies.¹⁴⁻¹⁶

Tumour size has been classed as a category I prognostic marker in the College of American Pathologists Consensus Statement 1999 with known prognostic implications in breast cancer.¹⁷ A larger tumour size is associated with usually advanced stage of presentation. This study shows a dismal picture with a small decrease in the tumour size at presentation over the last decade. There were 52% cases in the study by Malik et al which were <5cm in size while at present there are 69.4% cases with <5cm tumour size.¹⁰ This difference is statistically significant better diagnostic facilities and awareness may have contributed to the fact that 18.8% cases presented with a tumour size less than 2 cm while this percentage used to be only 8% in the study by Malik et al.¹⁰ Data from Southern Pakistan in a study by Siddiqui et al also shows a similarly poor picture with a small number of patients (5.5-7%) having a tumour size of <2cm.¹⁸

It is of the utmost importance to note that whereas in the western world the proportion of early breast cancer diagnosed as ductal carcinoma in situ (DCIS) has increased from 2.8% in 1973 to 14.4% in 1995, due to widespread screening mammography, in our study not a single case was diagnosed as DCIS. This is stage 0 disease which is the precursor for invasive cancer and has an excellent prognosis. A study from a premier large private hospital in Karachi also reports <1% frequency of DCIS.¹⁹

Lymph node negative patients have a very good survival since only 20-30% patients develop recurrence within 10 years as compared with 70% recurrence in those with axillary lymph node involvement. In our material the number of node negative cases has remained about the same making up 25% cases and no significant difference was seen. The number of lymph nodes involved also determines the surgical stage and involvement of 4 or more lymph nodes carries a relatively poor prognosis.¹⁶ Wahid et al⁹ and the present study show 29% and 35.6% cases respectively in the category having 1-3 lymph nodes involved. More than 60% patients had more than 4 involved lymph nodes showing a slight decrease compared to the previous decades which was not statistically significant.⁸

WHO Classification of tumours has defined the specific subtypes of breast carcinoma with diagnostic criteria for each entity.⁸ Infiltrating ductal carcinoma has been the commonest diagnosis in more than 90% patients previously but in the current study it made up 80.8% of the total cases comparable with another recent study.¹⁶

Approximately 13% cases of different specific entities were diagnosed including medullary carcinoma, mucinous carcinoma, papillary carcinoma, metaplastic carcinoma and tubular carcinoma and 6% cases of infiltrating lobular carcinoma were also seen. It can be appreciated that these entities were usually lumped together in the infiltrating ductal carcinoma in the past in the absence of specific diagnostic criteria and immunohistochemistry.⁸ Since these have definite prognostic implications efforts should be made to classify them accurately.

Tumour grade is an important determinant which allows risk stratification within a given stage of carcinoma.¹⁷ In our earlier study, grade 3 tumours constituted 62% of the total tumours.¹⁰ Subsequently in 1998 and at present grade 2 tumours constitute the majority of more than 60% cases which is also the observation by Siddiqui et al in Southern Pakistan.¹⁸ However no statistically significant difference was seen in the grade of the tumours over the three decades.

Paget's disease and skin involvement are seen with high grade advanced carcinomas.⁸ There were 36% cases showing nipple, dermal and epidermal invasion in the present study which was 21% in the earlier studies showing a

significant increase. Another local study also shows 29.3% cases with skin involvement.¹⁵ Dermal invasion has been included in the minimum data set for reporting breast cancers by National Health Service²⁰ (NHS) of the United Kingdom which may be the reason of reporting of this higher frequency.

Conclusion

The results of the present study in comparison with those over the past two decades and other similar studies in the region are not very encouraging. The age of presentation remains younger as compared to the West. However, a positive note is seen in terms of a decreasing tumour size due to relatively earlier presentation in some cases. Furthermore, specific guidelines for prognostic markers by NHS, College of American Pathologists (CAP) and World Health Organisation (WHO) have also helped us to stratify the prognostic markers like dermal or nipple involvement and specific histological type which may alter the treatment protocols with prognostic implications, a practice which was absent in the past. The lack of cases of DCIS in our material underlines the need for mammography and effective screening programmes.

Recommendation

There is a dire need to launch an effective screening programme at the national level with active involvement of gynaecologists, family physicians, lady medical officers and lady health visitors which would definitely lead to earlier detection of cases. Breast self-examination and ultrasound examination should be promoted and adopted as a first line investigation in comparison to mammography. The effectiveness of the above measures may be judged in future taking the prognostic parameters ascertained in this study as the baseline.

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