International Surgery Journal
Kumar K et al. Int Surg J. 2019 Apr;6(4):1323-1326
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20191270

Original Research Article

Breast cancer: correlation of receptor status with clinical presentation, stage of disease, histopathological grade and short term outcome

Kanav Kumar, Murtaza Akhtar*, Murtuza Rangwala

Department of Surgery, NKP Salve Institute of Medical Sciences and Research Centre and Lata Mangeshkar Hospital, Nagpur, Maharashtra, India

Received: 24 January 2019
Accepted: 28 February 2019

***Correspondence:**
Dr. Murtaza Akhtar,
E-mail: murtazaakhtar27@gmail.com

ABSTRACT

Background: Breast cancer is the commonest female cancer representing a quarter of all cancers worldwide. An important development in breast cancer management was the realization of role of hormone receptors in disease. Thus, the present study was carried out to evaluate the receptor status and its correlation with clinical presentation, stage, grade and short term outcome.
Methods: All female patients with lump in breast confirmed as breast cancer were included and their receptor status was evaluated using immunohistochemistry.
Results: A total of 147 patients with a mean age of 50.16±12.08 years were enrolled. Almost half of the patients (48.3%) of the patients were found to have locally advanced breast cancer. Of the 147 patients, 91.49% tumours were either Nottingham grade 2 or 3. Triple negative breast cancer (TNBC) was the commonest subtype seen in 43.54% patients. On correlating the results with receptor status, it was found that TNBC patients were younger than HER2neu positive and ER PR positive patients. Also, TNBC patients had a longer duration of lump and the lump was of larger size at presentation. On correlating receptor status with tumour biology it was seen that more than half (54.69%) of the patients who were triple negative had a grade 3 tumour and poorer disease free survival and overall survival.
Conclusions: In conclusion it is seen that TNBC forms a majority of the cases in the central Indian population with more aggressive presentations and outcomes. Absence of any targeted therapies against them leads to a worse DFS and overall survival.

Keywords: Breast cancer, Receptor status, Triple negative breast cancer, Nottingham grade, Locally advanced breast cancer

INTRODUCTION

Breast cancer is the commonest female cancer representing a quarter of all cancers worldwide.[1] In Indian women age adjusted incidence rate is 25.8 per 100000.[2] India is facing challenging situations due to an 11.5% increase in incidence and 13.2% increase in mortality due to breast cancer between 2008-2012.[1,3] The reason for increase in mortality is due to more patients presenting with locally advanced disease which is due to absence of an established breast cancer screening program and poor medical facilities. An important development in breast cancer management was the realization of presence of hormone receptors in tumour tissue and its correlation with hormonal therapy, chemotherapy and prognosis.[4] Ovarian steroids are necessary for breast development and an imbalance initiates abnormal processes like epithelial hyperplasia, intra-ductal and invasive carcinoma.[5] The information of receptor status of breast cancer patients in central India is very limited. Hence, this study was carried out to evaluate the receptor status and its correlation with

clinical presentation, stage of disease, histopathological grade and short term outcome of breast cancer patients in central India.

METHODS

This was a longitudinal observational study carried out between December 2013 and November 2018 in the Department of Surgery in NKP Salve Institute of Medical Sciences and Lata Mangeshkar Hospital, Nagpur. The inclusion criteria was all female patients presenting with lump in breast that was histopathologically or cytologically confirmed cases as breast cancer. Patients previously treated for breast cancer and presenting with metastatic disease were also included. Cases of phylloides tumour, lymphoma of breast and sarcoma of breast were excluded from the study. All the cases were immunohistochemically evaluated for estrogen and progesterone and HER2neu receptor status. Using a proforma various factors such as age, clinical presentation, stage of disease, receptor status histopathological grade, management and short term outcomes were studied. The data recorded was entered into an excel sheet and analysed using statistical software STATA version 10.1, 2011. Inferential statistics included tests of significance and tests of association. Two independent sample t test were used to assess significance of difference in two comparison groups. Pearson chi square test was applied to test association between outcome and predictor variables. Fischer's exact was used for small sample size. P<0.05 was considered statistically significant.

RESULTS

A total of 147 patients with a mean age of 50.16±12.08 years and a range of 26 to 94 years were enrolled. Almost one-third (29.93%) of the patients were in the age group of 40-50 years while 42 (28.57%) patients were less than 40 years of age. The remaining (41.5%) patients were above the age of 50 years. Six (4.08%) of the patients were nulliparous. Seven (4.76%) patients had a family history of breast cancer in a first degree relative. Of the 147 patients, 144 (97.95%) patients presented with a predominantly painless breast lump while the remaining 3 (2.05%) patients were previously diagnosed cases of breast cancer who had undergone mastectomies and presented with metastatic disease. The mean duration of the breast lump was 6.59±8.21 months. The mean size of the lump at presentation was 4.97×4.36 cms. Only fifteen (10.2%) patients had a history of nipple discharge. Right sided cancers were predominant seen in 80 (54.42%). Lumps were most frequent in the upper outer quadrant (45.14%) followed by the upper inner quadrant (22.92%). Based on the TNM classification, patients were sub classified into early breast cancer (EBC), locally advanced breast cancer (LABC) and advanced breast cancer (ABC). Almost half of the patients (48.3%) of the patients were found to have LABC while 40.82% patients had EBC and the remaining 10.88% had ABC (Table 1).

On histopathological examination of the tumour, it was found that infiltrating ductal carcinoma was the commonest type seen in 87.07% patients followed by infiltrating lobular carcinoma in 6.12% patients. On evaluation of tumours using Nottingham grade it was found that 91.49% tumours were either grade 2 or 3 suggestive of an aggressive malignancy. All tumours were evaluated immunohistochemically for their receptor status and it was found that Triple negative breast (TNBC) was the commonest subtype seen in 64 (43.54%) patients, while 43 (29.25%) patients were found to be only Hormonal receptor positive and the remaining 40 (27.21%) patients were found to be HER2neu positive (Table 2).

Table 1: Distribution of study subjects according to stage of disease.

Stage of disease	No. of patients (%)
Early breast cancer	
Stage I [T1 N0 M0]	60 (40.82)
Stage IIA [T1 N1 M0, T2 N0 M0]	
Stage IIB [T2 N1 M0, T3 N0 M0]	
Locally advanced breast cancer	
Stage IIIA [T1 N2 M0, T2 N2 M0, T3 N1 M0, T3 N2 M0]	71 (48.3)
Stage IIIB [T4 N0 M0, T4 N1 M0, T4 N2 M0]	
Stage IIIC [Any T N3 M0]	
Advanced breast cancer	
Stage IV [Any T Any N M1]	16 (10.88)
Total	147 (100)

Table 2: Receptor status of study subjects.

Receptor status	No. of patients (%)
Triple negative breast cancer (TNBC)	64 (43.54)
Only ER PR positive	43 (29.25)
HER2neu positive	40 (27.21)
Total	147 (100)

On carrying out analytical statistics of the three receptor groups, it was observed that patients who were HER2neu positive were older and TNBC patients were younger as compared to hormone receptor positive patients. This finding was found to be statistically significant (p<0.05). It was found that TNBC patients had breast lumps of longer duration and were of a larger size at the time of presentation and this difference in the size was found to be statistically significant (Table 3). More than half of the cases of LABC and ABC enrolled in the study were found to be triple negative but this was not found to be statistically significant (p>0.05) (Table 4). More than half of the TNBC patients (54.69%) were found to have On correlating the receptor status with Nottingham Grading on histopathology it was found that 30 (61,43%) out of

42 ER PR positive patients were in grade 1 and 2,while 36 (94.73%) out of 38 patients of HER2 neu were in grade 2 and 3.Similarly 61 (95.32%) TNBC patients were classified as into grade 2 and 3 patients and this was found to be statistically significant (p<0.05) (Table 5). TNBC patients showed a higher recurrence rate (9.09%) and higher mortality rate (7.81%) during the short follow up period but this was found to have no statistical significance.

Table 3: Correlation of receptor status with age and clinical presentation.

Receptor status	Mean age (years)	Mean duration of lump (months)	Mean size at presentation (horizontal)	Mean size at presentation (vertical)
ER PR positive	51.3±14.24	5.14±5.57	4.41±1.79 cm	3.79±1.39 cm
HER2neu positive	53.2±10.69	6.28±8.09	4.89±2.05 cm	4.36±1.88 cm
TNBC	47.5±10.88	7.72±9.57	5.38±2.01 cm	4.73±2.11 cm
P value	<0.05 (S)	0.278 (NS)	<0.05 (S)	<0.05 (S)

Table 4: Correlation of receptor status with stage of disease.

Stage of disease	ER PR positive	HER2neu positive	TNBC	Total	P value
	N (%)	**N (%)**	**N (%)**	**N (%)**	
EBC	22 (36.67)	20 (33.33)	18 (30)	60 (100)	
LABC	19 (26.76)	15 (21.13)	37 (52.11)	71 (100)	0.061 (NS)
ABC	2 (12.5)	5 (31.25)	9 (56.25)	16 (100)	

Table 5: Correlation of receptor status and Nottingham grade.

Nottingham grade	ER PR positive	HER2neu positive	TNBC
	N (%)	**N (%)**	**N (%)**
1	7 (16.67)	2 (5.27)	3 (4.68)
2	23 (54.76)	21(55.26)	26 (40.63)
3	12 (28.57)	15 (39.47)	35 (54.69)
Total	42 (100)	38 (100)	64 (100)
P value	<0.05 (S)		

DISCUSSION

Breast cancer is the commonest site specific cancer in women and a leading cause of cancer related deaths in women aged 20-59 years. It accounts for 26% of all newly diagnosed cancers in women and 15% of cancer related deaths in them.[6] Rising incidence of breast cancer in Indian scenario prompted us to evaluate the receptor status of tumour tissue by immunohistochemistry and correlate it with clinical features, staging and tumour biology as assessed by Nottingham grade. It was also correlated with overall disease free survival.

The mean age of presentation in the present study was 50.16±12.08 years which are earlier than western population but consistent with Indian statistics.[6-9] Apart from early age of occurrence of breast cancer almost half of the patients (48.3%) presented with LABC. This advanced presentation could be due to lack of awareness which in turn cause delay in getting surgical consultation or due to aggressive tumour biology.[10] The present study correlated receptor status of the malignancy with clinical and pathological parameters to assess this factor in Indian population. It was also observed in the present study that a majority (43.54%) of these patients were TNBC which are known to have aggressive tumour biology. On correlating our results with receptor status, it was found that TNBC patients were younger than HER2neu positive and ER PR positive patients and this correlates with the findings of Singh et al that triple negative breast cancers decline as age increases.[11] It was observed that TNBC patients had a longer duration of lump and the lump was of larger size at presentation. These findings were consistent with Nabi et al and Onitilo et al who found that ER PR positive tumours tend to be smaller.[12,13] On correlating receptor status with the stage of disease, it was found that a majority of LABC and ABC were triple negative although this was not statistically significant. Onitilio et al found that ER PR positive patients present at earlier stage of disease.[13] On correlating receptor status with tumour biology assessed with Nottingham grading, more than half (54.69%) of the patients who were triple negative had a grade 3 tumour. This correlation was statistically significant. Most of the studies in literature suggest ER PR positivity is associated with a lower grade while TNBC and HER2neu positive cancers are associated with a higher grade. Sofi et al found that ER PR positivity is associated with decreased breast cancer mortality.[12] Onitilo et al found that TNBC has the worst

overall survival and disease free survival. The DFS curve in TNBC was found to plateau after the 2nd and 3rd year but it continues downward in HER2neu positive cases.[13] These findings correlate with the findings of the present study that TNBC had the worst disease free survival and overall survival.

CONCLUSION

Triple negative breast cancer forms a majority of the cases in the central Indian population and is found in younger patients who present with larger breast lumps of longer duration and at more advanced stages with a higher Nottingham grade. This along with the absence of any targeted therapies against them leads to a worse DFS and overall survival. Thus there is an urgent need to develop awareness, screening programmes and newer treatments to combat the rising mortality in the Indian population.

ACKNOWLEDGEMENTS

We hereby acknowledge Dr Kajal Mitra, Dean, NKPSIMS, Nagpur for permitting us to publish this research. Sincere thanks to Dr Suresh Ughade for statistical support.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. International journal of cancer. 2015;136(5):359-86.
2. Gupta A, Shridhar K, Dhillon PK. A review of breast cancer awareness among women in India: Cancer literate or awareness deficit? Eur J Cancer. 2015;51(14):2058-66.
3. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010;127(12):2893-917.
4. Hawkins RA, Roberts MM, Forrest AP. Oestrogen receptors and breast cancer: current status. British J Surg. 1980;67(3):153-69.
5. Mori I, Yang Q, Kakudo K. Predictive and prognostic markers for invasive breast cancer. Pathology Int. 2002;52(3):186-94.
6. Ammaji DS, Suvarchala DA, Yogesh D. To study the clinical and pathological staging of breast cancer and to correlate these findings with status of the tumor markers. Paripex-Indian J Res. 2018;6(4):13-6.
7. Hathila TN, Sangle RB, Doshi SA, Firdaus DA, Rupani MP. A prospectivestudy of estrogen, progestrone and HER2neu receptor in cases of breast cancer in a tertiary care hospital of Bhavnagar, Gujarat, Western India. National J Med Res. 2015;5(3):185-9.
8. Takalkar UV, Asegaonkar SB, Kulkarni U, Kodlikeri PR, Kulkarni U, Saraf M, et al. Clinicopathological profile of breast cancer patients at a tertiary care hospital in marathwada region of Westen India. Asian Pac J Cancer Prev. 2016;17(4):2195-8.
9. Balasubramaniam S, Rotti S, Vivekanandam S. Risk factors of female breast carcinoma: a case control study at Puducherry. Indian J Cancer. 2013;50(1):65.
10. Akhtar M, Akulwar V, Gandhi D, Chandak K. Is locally advanced breast cancer a neglected disease? Indian J Cancer. 2011;48(4):403.
11. Singh R, Gupta S, Pawar SB, Pawar RS, Gandham SV, Prabhudesai S. Evaluation of ER, PR and HER-2 receptor expression in breast cancer patients presenting to a semi urban cancer centre in Western India. Journal Cancer Res Therap. 2014;10(1):26.
12. Sofi GN, Sofi JN, Nadeem R, Shiekh RY, Khan FA, Sofi AA, et al. Estrogen receptor and progesterone receptor status in breast cancer in relation to age, histological grade, size of lesion and lymph node involvement. Asian Pacific J Cancer Prev. 2012;13(10):5047-52.
13. Onitilo AA, Engel JM, Greenlee RT, Mukesh BN. Breast cancer subtypes based on ER/PR and Her2 expression: comparison of clinicopathologic features and survival. Clinical Med Res. 2009;7(1-2):4-13.

Cite this article as: Kumar K, Akhtar M, Rangwala M. Breast cancer: correlation of receptor status with clinical presentation, stage of disease, histopathological grade and short term outcome. Int Surg J 2019;6:1323-6.