



## Evaluation of Hormone receptor status in patients with operable breast cancer: a retrospective study at a Regional Cancer Centre in Northeast India

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### Abstract

**Background:** In India, Breast cancer is the most common cancer in female and hormone receptor status is an important prognostic and therapeutic tool in the management of breast cancer. So this study was done with the aim to evaluate the hormone receptor status in patients with operable breast cancer at a Regional Cancer Centre in Northeast India.

**Methodology:** This study is a retrospective case series study on 180 cases of operable breast cancer who were registered at Regional Cancer Centre, Regional Institute of Medical Sciences (RIMS), Manipur State after histopathological confirmation during the period from September 2015 to August 2018 and patients were reviewed for age, tumour size and metastatic lymph nodes positivity, histopathology, grading, hormone receptor status, staging and menstrual status.

**Results:** Overall 180 patients was studied and evaluated for hormone receptor status. 90 cases (50.0%) were both ER-/PR-, 66 cases (36.7%) were both ER+/PR+, 14 cases (7.8%) were ER+ and 10 other cases (5.5%) were only PR+. The mean age of presentation was  $52.6 \pm 0.82$  yrs and the number of patients reaches a peak between 31 - 50 years (59.4%). Maximum patients were found to be in poor socio-economic class. Invasive duct carcinoma (96.1%) was predominant histology. Majority of the cases (84.5%) had grade-III tumour. 17.8% of total patients presented in stage-I, 42.8% in stage-II and 39.4% in stage-III.

**Conclusion:** In Northeast India, incidence rate of breast cancer among younger age group has been increasing and more patients were ER/PR negative. Maximum numbers of grade-III tumour were found to be ER/PR negative and as the tumour size increased, ER/PR negativity also increased.

**Keyword:** Breast cancer, Hormone receptor, Northeast India.

### Introduction

In more developed regions, breast cancer is the second cause of cancer death after lung cancer<sup>1</sup>

but it is the most frequent cause of cancer death in less developed region. Even though, incidence rate of breast cancer in India is much lower compared

with western countries<sup>2</sup> it is now the most common cancer in women and recently overtaken cervical cancer.<sup>3</sup> Similarly, incidence rate of breast cancer has been increasing in Manipur and it is the commonest cancer in females in this region.<sup>4</sup>

Moreover, pathological parameters such as tumour size, histological subtypes, grade, status of hormone receptors, her 2 neu expression and lymph node are useful as prognostic factors in the management of breast cancer.<sup>5,6,7,8,9,10,11</sup>

Since hormone receptor status is an important predictive and prognostic factor, determination of hormone receptor status in patients with breast cancer before starting treatment is now a standard practice.<sup>12</sup> The hormone receptors (HR) best studied in breast cancer are estrogen receptor (ER) and progesterone receptor (PR).<sup>13</sup> Survival and response to hormone therapy are most favourable among women with tumors positive for both ER and PR expression, intermediate for tumours discordant on receptor status and least favourable for tumors negative for both.<sup>14</sup> In view of the existence of well established correlation between hormone receptor status with patient treatment response, survival, the threat breast cancer poses and unavailability of any published report on hormone receptors from this region, the present study had been conducted to evaluate hormone receptor status in relation to age, stage, primary tumour size, histology, grading and lymph node positivity to create a database of breast cancer patients in Manipur.

## Methods

This study is a retrospective case series study on 180 cases of operable breast cancer who were registered at Regional Cancer Centre, Regional Institute of Medical Sciences (RIMS), Manipur State after histopathological confirmation during the period from September 2015 to August 2018 and case notes of those 180 patients were reviewed for clinical presentation like ages, tumour size and metastatic lymph nodes positivity, histopathology, grading, hormone receptor status, staging and menstrual status. The

patients were staged according to the TNM staging system (AJCC 7<sup>th</sup> Edition). 180 patients had undergone either modified radical mastectomy or breast conserving surgery followed by adjuvant chemotherapy and radiation. Cases without complete information and unknown hormone receptor status were excluded in the present study. An approval from the Institutional Ethics Committee for research involving human subjects was obtained before the study was conducted. Confidentiality of the patient's identity was maintained. The data were analyzed using SPSS 21 and descriptive statistics was used as type of statistical analysis test. Tumour tissue was subjected to routine processing and sections were stained with H&E. The histopathological sections were diagnosed based on WHO classification and graded adopting Modified Blooms Richardson grading system.

The formalin fixed, paraffin embedded tissues were subjected to ER and PR expression study. Specimens had been processed by the Horse Radish Peroxidase method. Protein retrieval had been done by microwave technique. The following antibody clones had been used: 1. Mouse anti-human ER alpha1D5, 2. Mouse anti-human PR clone PgR636.

Only nuclear staining pattern was considered positive for ER expression (ER+) and PR expression (PR+). A positive staining was defined when at least 1% of the tumour cells take up the nuclear stain of any intensity. Breast ductal epithelial cells acted as internal controls. ER, PR staining was quantified by using Allred score. All the slides were quantified by combining proportional score based on the percentage of cells showing nuclear stain and intensity score based on intensity of staining.

### The Proportional Score (PS) is as follows:

0 = No staining

1 = <1% of cells showing nuclear stain

2 = 1%- 10% cells showing nuclear stain

3 = 11%-33% cells showing nuclear stain

4 = 34%-66% cells showing nuclear stain

5 = 67%- 100% cells showing nuclear stain

**Intensity score (IS) is as follows:**

- 0 = No staining  
 1 = Weak staining  
 2 = Intermediate staining  
 3 = Strong staining

**Total Score (TS):** sum of proportional score + intensity score.

Scores of 0 and 2 were considered negative and scores of 3 to 8 were considered positive.

**Results**

As shown in Table-1, among 180 patients, 100 patients (55.6%) were illiterate and only 18 (10.0%) patients were from higher socio-economic status (Class-I and II). 50.0%, 30.0%, and 10.0% of the total 180 patients were found to be in poor socio-economic classes-III, IV and V respectively. Among the patients, the ages ranged from 28 to 76 yrs. The mean age of presentation was  $52.6 \pm 0.82$  yrs. The number of patients reaches a peak between 31 - 50 years (59.4%), then begins to decline in the age group of 51-76 years (32.2%) as shown in Table-1. 109 patients (60.6%) were post menopausal patients.

Mean size of the breast tumour was 7.0 cm diameter, ranging from 1 cm to 14 cm. 16.1% of tumour size were <2 cm, 46.7% were between 2-5 cm and 37.2% were >5 cm. The histological classification revealed a predominance of invasive duct carcinomas (96.1%) followed by lobular carcinomas (2.8%) and medullary carcinomas (1.1%). Majority of the cases (84.5%) had grade-III tumour followed by grade-II (14.4%) and grade-I (1.1%) respectively.

Only 17.8% of total patients presented in stage-I, 42.8% in stage-II and 39.4% in stage-III respectively. During surgery, 1 to 3 nodes (41.5%), 4 to 10 nodes (33.5%) and more than 10 nodes (25.0%) of axillary lymph nodes were removed. Mean number of involved nodes was 5 (range: 1-27). 90 cases (50.0%) were both ER-/PR-, 66 cases (36.7%) were both ER+/PR+, 14 cases (7.8%) were ER+ and 10 other cases (5.5%) were only PR+.

**Table-1:** Patient characteristics (n=180)

Variables	Frequency	Percentage (%)
<b>AGES (YEARS)</b>		
Less than 30	10	5.6
31-50	107	59.4
51-70	58	32.2
Above 70	5	2.8
<b>SOCIO ECONOMIC STATUS</b>		
I	7	3.9
II	11	6.1
III	90	50.0
IV	54	30.0
V	18	10.0
<b>EDUCATION LEVEL</b>		
Illiterate	100	55.6
Primary education	18	10.0
Secondary education	33	18.3
Above secondary education	29	16.1
<b>MENSTRUAL STATUS</b>		
Pre-menopausal	71	39.4
Post-menopausal	109	60.6
<b>HISTOPATHOLOGY</b>		
IDC-NOS	173	96.1
Medullary	2	1.1
ILC	5	2.8
Others	0	
<b>HISTOLOGICAL GRADE</b>		
I	2	1.1
II	26	14.4
III	152	84.5
<b>STAGING (TNM Staging-AJCC 7<sup>th</sup> edition)</b>		
I	32	17.8
II	77	42.8
III	71	39.4
IV		

**Table-II:** Hormone receptor status in relation to age, tumour size, stage, histology, grading, lymph node positivity (n=180)

Variable	Hormone receptor status			
	No (%)			
	ER+/PR+	ER+/PR-	ER-/PR+	ER-/PR-
<b>Number of Patients</b>	66 (36.7%)	14 (7.8%)	10 (5.5%)	90 (50.0%)
<b>Age</b>				
<30	3 (30.0%)	2 (20.0%)	1 (10.0%)	4(40.0%)
31-50	43 (40.2%)	7 (6.5%)	5 (4.7%)	52 (48.6%)
51-70	20 (34.4%)	3 (5.2%)	3 (5.2%)	32 (55.2%)
>70	-	2 (40.0%)	1 (20.0%)	2 (40.0%)
<b>Stage</b>				
I	20 (62.5%)	-	1 (3.1%)	11 (34.4%)
II	30 (38.9%)	8 (10.4%)	6 (7.8%)	33 (42.9%)
III	16 (22.5%)	6 (8.5%)	3 (4.2%)	46 (64.8%)
<b>Primary tumour size</b>				
<2	16 (55.2%)	3 (10.4%)	3 (10.4%)	7 (24.1%)
2-5	40 (47.6%)	7 (8.3%)	4 (4.8%)	33 (39.3%)
>5	10 (14.9%)	4 (6.0%)	3 (4.5%)	50 (74.6%)
<b>Lymph node positivity</b>				
<4	38 (32.8%)	8 (6.9%)	8 (6.9%)	62 (53.4%)
>4	28 (43.8%)	6 (9.3%)	2 (3.1%)	28 (43.8%)
<b>Histopathology</b>				
IDC-NOS	63 (36.4%)	14 (8.1%)	10 (5.8%)	86 (49.7%)
Medullary	-	-	-	2 (100.0%)
ILC	3 (60.0%)	-	-	2 (40.0%)
<b>Histological grading</b>				
1	1 (50.0%)		1 (50.0%)	-
2	22 (84.6%)	1 (3.9%)	-	3 (11.5%)
3	43 (28.3%)	13 (8.6%)	9 (5.9%)	87 (57.2%)

## Discussion

Breast cancer is a biologically heterogeneous disease and has been one of the most heavily researched areas, not only in terms of its increasing incidence but also more and more understanding of its biological behaviour resulting in large evolving treatment paradigm. Suzuki T et al<sup>15</sup> showed that ER+ breast cancers have a lower incidence of recurrence and a longer disease free interval regardless of tumour size or lymph node status. Thus, there is paramount importance of knowing ER/PR status of patients before starting any form of treatment.

In this present study, 55.6% patients were illiterate which is almost similar to other studies in India<sup>16,17</sup> and only 18 patient (10.0%) were from higher socio-economic status (Class-I and II). 50.0%, 30.0%, and 10.0% of the total 180 patients were found to be in poor socio-economic classes-

III, IV, and V respectively. So in comparison to a study in Madhya Pradesh, more patients in our study were from very low socio-economic status family.<sup>17</sup>

In this study, majority of the patients (59.4%) were in the age group of 31-50 years, similar to the findings of previous studies in other high-incidence regions in southern india.<sup>18</sup> In contrast to our findings, 37-42.0% of the patients belonged to the age group of 41-50 years in maximum studies of India.<sup>16,17,19,20</sup> Moreover, in few other studies in India<sup>21,22,23</sup> 48-54% of the patients were in the age group of 40-60 years. Out of total 180 patients, 90 patients (59.4%) were in the age group of 31-50 years and ER-/PR- was found in 52 patients (48.6%). It was observed that as the age increases, ER positivity of our patients does not increase in contrast to other Indian study.<sup>24</sup>

ER+ tumour in premenopausal and postmenopausal patients was found to be 39.4% and 47.7% respectively. Difference of ER positivity with respect to menopausal status in our study is not statistically significant (P-value = 0.275) similar to a study by Gautham Ranjan et al.<sup>25</sup> But our study result is not in concordance with the study findings of an earlier study of Kaul R et al<sup>26</sup> where the statistically significant difference in ER positivity was observed.

On further evaluation, increasing number of patients with ER negativity in respect to increasing stage was found in our study where ER negativity in stage I, Stage-II and Stage-III were 40.6%, 50.6% and 69.0% respectively.

Out of total 180 patients, most of the patients (46.7%) had tumour size of 2-5 cms and ER+/PR+ was observed in 47.6 % of them. In contrast to a study of Vedashree MK et al<sup>20</sup>, it was also observed that as the tumour size increases, ER/PR negativity increases where 24.1%, 39.3% and 74.6% of patients with ER/PR negativity had tumour sizes less than 2cm, 2-5cm and more than 5 cm respectively. In contrast to a study of Gulam Nabi Sofi et al<sup>27</sup>, increasing number of metastatic lymph nodes had decreasing ER/PR positivity in our study where ER/PR positivity were 43.8% and 32.8% in metastatic lymph node numbers less than 4 and more than 4 respectively.

Maximum numbers of grade-III tumour (57.3%) were found to be ER-/PR- showing more aggressive tumour behaviour. ER positivity trend was highest for grade-II tumour (88.5%) compared to grade-I (50.0%) and grade-III tumours (36.9%). Similarly PR positivity was more with grade-II (84.6%) compared to grade-I tumour (50.0%) and grade-III tumours (34.8%). Our findings are comparable to the study findings of Malaysian patients.<sup>28</sup> In contrast to our findings, majority of cases were grade-II (59.0%) and maximum tumours in grade-I were ER+(59.0%) and PR+ (37.0%) compared to grade-III and grade-II in a study from Nepal.<sup>29</sup> Invasive ductal carcinoma was the most common histopathology accounting for (96.1%) followed

by invasive lobular carcinomas (2.8%) and medullary carcinomas (1.1%) respectively similar to other Indian studies.<sup>16,17,23,30,31</sup> Similar to findings of Desai et al<sup>32</sup>, tumours of invasive duct carcinomas was predominantly ER-/PR-(49.7%) in our study.

In the present study, more number of patients (50.0%) were ER-/PR- and less number of patients (36.7%) were ER+/PR+ compared to the findings of few studies<sup>1,4,33</sup> where percentage of ER-/PR- ranged from 30.7 to 42.19% and ER+/PR+ patients ranged from 56.0% to 60.4%. 44.4% of our patients were ER+ whereas 34.5% of patients in Himalayan region of northern India were ER+.<sup>26</sup>

Overall ER-/PR-(50.0%) in our patients were comparable to the study findings of eastern Indian patients<sup>34</sup> but ER/PR negativity of Pakistani patients (30.6%) and Caucasian (21.8%) were less than our findings.<sup>35</sup>

In the present study, the overall ER+ was 44.4% and PR+ was 42.2% which were more than the reports from Malaysia and study findings of Desai et al.<sup>32</sup> But our findings were in contrast to the study findings from Indonesia<sup>36</sup> where overall ER+ was 52.1% and PR+ was 48.5%. In the present study, 42.2% of patients were PR+ while 55.0 % of the patients in the United States were PR.<sup>37</sup> Our study showed PR positivity of 42.2% which was comparable with other studies from India which had shown PR positivity at 42%<sup>39</sup> and 41.5%<sup>25</sup> but PR positivity in our study was more in comparison to few studies of Southern India (33.3%)<sup>38</sup> and Himalayan region (36.4%).<sup>26</sup>

### Conclusion

In this present study, majority of the patients were found to be illiterate and in poor socio-economic classes showing urgent need of awareness and screening programme in this region. It was observed that incidence rate of this cancer among younger age group has been increasing and as the age increases, ER positivity did not increase in contrast to other Indian study. Difference of ER positivity with respect to menopausal status was

not significant. Maximum numbers of grade-III tumour were found to be ER-/PR-. On further evaluation, increasing number of patients with ER- in respect to increasing stage was found. It was also observed that as the tumour size increased, ER/PR negativity increased. More patients were ER-/PR- and less patients were ER+/PR+. In view of the above findings, we feel that tumour biology of breast cancer in this particular region of India to be more aggressive compared with other Indian population. Further study on possible role of environmental, lifestyle, socio-demographic, ethnicity and genetic factors may be useful to further understand breast tumour biology of this region.

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