



## INCIDENCE OF HORMONE AND HER2NEU RECEPTORS IN PATIENTS OF CA BREAST IN WESTERN UTTAR PRADESH

### Surgery

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### KEYWORDS

#### INTRODUCTION

Worldwide, breast cancer is the most frequently diagnosed cancer and leading cause of death among females, accounting for 23% of total cancer cases and 14% of cancer deaths.<sup>1</sup> Breast cancer is the most common malignancy among women in the western world and in India second only to the carcinoma cervix.<sup>2</sup> This accounts for seven percent of the global burden of breast cancer and one-fifth of all cancers among women in India.<sup>3</sup>

Hormone receptor status acts primarily as a predictive factor for a tumour's response to therapeutic and adjuvant hormonal treatment.<sup>4,7</sup> Presence of any detectable ER is an indication for adjuvant endocrine therapy and either Tamoxifen or Tamoxifen with ovarian function suppression, is an accepted standard for treatment of pre-menopausal women with hormone-positive breast cancer.<sup>8</sup>

Salmon D J et al<sup>9</sup> first demonstrated the clinical efficacy of trastuzumab along with chemotherapy in HER positive breast carcinomas. In 2005, it was licensed for use in early breast cancer, after the results of the HERA (Herceptin Adjuvant) trial which showed that 1 year of trastuzumab therapy post-adjuvant chemotherapy treatment significantly improved the disease-free survival (DFS) of patients with HER2-positive disease.<sup>10</sup>

At 12th St.Gallen International Breast Cancer Conference held in 2011 at Switzerland a consensus classification of intrinsic subtypes of breast cancer has been proposed. They have incorporated four basic markers, ER, PR, HER2 and Ki 67 to classify the breast cancer subtypes.

They classified breast cancer subtype in:-  
Luminal A (ER and/or PR positive, HER2 negative and **Ki67<14%**)  
Luminal B HER2 negative (ER and/or PR positive, HER2 negative, **Ki67>14%**)  
Luminal B HER2 amplified (ER and/or PR positive, HER2 positive and **any Ki67**)  
HER 2 positive (HER 2 positive, ER and PR negative)  
Triple negative (ER, PR and HER2 negative)<sup>11</sup>

#### AIMS AND OBJECTIVES

To study the presence of ER, PR and HER2NEU receptors in patients admitted with ca breast.

To study the outcome of our study population based on ER, PR, HER2Neu receptor status

#### MATERIALS AND METHODS

##### Study design

This is a prospective and retrospective study in which cases will be selected taking the inclusion and exclusion criteria into consideration. Detailed history will be taken as per the prepared proforma followed by detailed and complete clinical examination.

##### Source of collection

All the patients with breast cancer coming to surgery OPD and getting admitted to Department of Surgery in SVBP hospital attached to LLRM Medical College, Meerut will be taken for study, considering the inclusion and exclusion criteria. Patients with ca breast attending SVBP hospital, Meerut during the period from august 1 2012 to july 31 2015 will be taken into retrospective study and from august 1, 2015 to july 31, 2017 in prospective study.

#### Inclusion criteria

All CA breast patients attending surgical OPD and /or admitted in surgical wards of L.L.R.M. Medical College and associated S.V.B.P. Hospital.

Females of all age groups are included.

#### Exclusion criteria

Male patients of CA breast.

All patients presenting with benign breast disease.

Patients unwilling to undergo the necessary investigations or surgical procedure.

Known cases of CA breast presenting with recurrence with previously unknown/known receptor status.

#### Methodology

Written and informed consent to be taken from all patients.

A complete work up will be performed which will include a detailed clinical history, along with relevant past, personal, family and treatment history.

All patients will be subjected to a thorough clinical examination with emphasis on the following-

History

Examination

Investigations- mammography, trucut needle biopsy, IHC staining.

Surgery- Modified radical mastectomy

Follow up

Interpretation of collected data.

Inference

#### OBSERVATION AND RESULT

In this prospective and retrospective study of 5 years (2012-2017), of cases of primary, previously untreated breast cancer, in female population of western Uttar Pradesh, a total of 408 cases were studied, presenting to our hospital. Of these 408 cases, 120 patients were included in the study based on inclusion and exclusion

**Table 1 : Immunohistochemical markers**

IHC class	Number of patients	Percentage (in %)
Luminal A (ER+, PR +, HER2neu -)	19	16%
Luminal B (ER +, PR +, HER2neu +)	16	13%
Her 2 neu +ve only (ER/PR -, her2neu overexpressive)	26	22%
Triple negative (ER-, PR-, her2neu-)	59	49%

Hence, maximum number of patients were from the triple negative category, 49%, followed by her2neu +ve tumors (35%) (luminal B+ her2neu only positive) as the second most common class.

Hormone receptors (ER, PR) were positive in only 29% of cases (luminal A+luminalB)

**Table 2 : Stage at presentation and its correlation with IHC class**

Stage of presentation	Luminal A	Luminal B	Her 2 neu +ve only	Triple negative
Early breast ca	14	09	17	32

LABC	03	04	06	19
Metastatic ca breast	02	03	03	08

P value- early breast cancer- 0.439, LABC- 0.519, metastatic cancer breast- 0.894. P value is insignificant.

**Table 3 : Distribution of patients as per stage of presentation in the respective IHC group**

Stage of presentation	Luminal A	Luminal B	Her 2 neu +ve only	Triple negative
Early breast ca	74%	56%	65%	54%
LABC	16%	25%	23%	32%
Metastatic ca breast	10%	19%	12%	14%

**Following observations were made-**

74% of luminal a tumors presented as early breast cancer, indicating towards better prognosis.

However, only 56% of luminal B tumors presented in early stage, indicating more aggressive disease with respect to luminal A.

46% of triple negative and 35% of her2neu +ve only tumors presented as locally advanced or metastatic breast cancer, indicating towards more aggressive course of disease.

**Table 4 : Correlation between outcome and IHC class**

Outcome	Luminal A	Luminal B	Her 2 neu +ve only	Triple negative
No recurrence	15	10	12	34
Bone metastasis	02	02	01	07
Local recurrence	Nil	Nil	02	05
Visceral metastasis	00	01	01	02
Visceral+bone metastasis	Nil	Nil	04	01
Expired	Nil	01	02	01

\*excluding patients lost to follow up.

**Recurrence rates in various IHC groups-**

Luminal A - 12% of cases. All the patients who presented with metastasis from this subclass, had metastasis to bone. No cases of visceral metastasis were reported.

Luminal B – 29% , with metastasis to both bone and viscera.

Her 2 neu +ve only – 50%

Triple negative group- 32%, with metastasis to bone and viscera. Shows special propensity of metastasis to brain.

**LOCAL RECURRENCE**

Seen in 07 patients, making it approximately 8% of the total cases.

Initial stage of presentation was 2A and 2B for 2 patients each, and 3B for rest 3 patients.

Most common IHC subclass associated with local recurrence was found to be triple negative, seen in 71% of patients followed by only her 2 neu overexpressive (ER, PR –ve).

4 patients received radiation previously whereas 3 patients did not receive any such treatment.

**DISCUSSION**

The aim of our study is to study the presence and prevalence of estrogen, progesterone and her2 neu receptors and the outcome of primary cases of cancer breast presenting to our hospital.

The results of our study were compared to similar studies done in past in terms of percentage of hormone receptor

Study	Desai et al <sup>16</sup>	Rao et al <sup>17</sup>	Sandhu et al <sup>24</sup>
% of patients with +ve ER + PR status	32.4%	36.5%	48%
Malyani et al <sup>18</sup>	Rajan et al <sup>19</sup>	Our study	
60.6%	56%	29%	

Hence, incidence of hormone receptor positive tumors is found to be lower in our study population as compared to other studies done elsewhere.

**Her2neu receptor positive tumors**

Sandhu et al <sup>24</sup>	Puvitha et al <sup>23</sup>	Malyani et al <sup>18</sup>	Our study
27%	22%	30.8%	35%

Hence, the results of our study are similar as compared to other studies done in past, and it can be concluded that prevalence of her2 neu receptors is 35% in our population.

**Triple negative tumors**

Puvitha et al <sup>23</sup>	Rao et al <sup>17</sup>	Sandhu et al <sup>24</sup>	Our stuPatnayak et al <sup>21</sup>
49%	50%	31%	22.7%
Basu et al <sup>20</sup>	Den et al <sup>15</sup>	Our study	
14%	11.2%	49%	

Also, Murtaza et al<sup>22</sup>, stated that that, the most common IHC class in their study was found to be triple negative tumors. Hence, it could be concluded that the prevalence of triple negative tumors is quite high in our population, representing 49% of these patients.

**Recurrence rates in various IHC groups as seen in our study, are as follows-**

Luminal A - 12% of cases. All the patients who presented with metastasis from this subclass, had metastasis to bone. No cases of visceral metastasis were reported. This is in concordance to the observation that bony metastasis is more common in luminal A subgroup<sup>12,13</sup>

Luminal B – 29% , with metastasis to both bone and viscera.

Her 2 neu +ve only – 50%, hence indicating more aggressive disease in this subclass.

Triple negative group- 32%, with metastasis to bone and viscera. Shows special propensity of metastasis to brain. Similar observation was made by Jochen et al<sup>14</sup>, who proposed that all the patients who presented with brain metastasis after relapse were found to be triple negative.

Local recurrence is seen in 8% of cases in our study. This is almost double the cases as reported by Basavalinga et al<sup>25</sup>. Of the cases with local recurrence, 71% of cases were found to be triple negative in our study whereas rest were her2neu receptor only positive. A similar study done by Xingrao et al<sup>26</sup> stated that local recurrence is highest in the triple negative group and lowest in luminal A subgroup. Therefore, the higher number of local recurrences could be attributed to the more number of triple negative cases seen in our study as compared to other studies.

**CONCLUSION**

To conclude, in this study of previously untreated primary cases of cancer breast of western Uttar Pradesh, triple negative breast cancer is found to be most common IHC subtype followed by her2neu receptor only positive subtype as the second most common subclass, with relatively lower expression of hormone receptors, in the study population. This pattern is found to be similar to the other studies done in various parts of the country, although, a change in trend is seen when compared to studies from the western countries where there is more expression of the hormone receptors. Relapse rate is found to be highest in her2neu receptor only positive subgroup indicating towards a more aggressive disease in this subset of patients.

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