

**Research Article****Hormone receptor sensitivity in Breast Cancer patients in Pune city of Maharashtra State, India – A retrospective study**

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**ABSTRACT:**

**Introduction:** Breast cancer is the most frequently diagnosed cancer in women both in developed and developing countries. In the year 2011 over 508000 women died because of breast cancer. Every year about 75,000 new cases of breast cancer have been reported by the World Health Organization. The incidence in India is also high. The National Cancer Registry has reported a rate of 25 to 30 per 100,000 women per year in cities like Bombay and Delhi. **Method:** A hospital based study was done to scrutinize the various histo-pathological facets of breast cancer patients. The size of the sample was 37 subjects. Range of age group was between 30 to 70 years for females. The patients were classified according to the Nottingham's score, grading, and immune-histo-chemistry marker study. They were further divided into different hormone receptor sensitivity groups like estrogen receptor sensitivity, progesterone receptor sensitivity and HER2Neu sensitivity group.

**Key words:** Breast cancer, Nottingham's score, immunohisto-chemistry marker, hormone receptor sensitivity.

**INTRODUCTION:**

Breast cancer is the most frequently diagnosed cancer, accounting for 23% of total cancer cases and 14% of cancer deaths. Every year about 75,000 new cases of breast cancer have been reported by the World Health Organization (Global Health Estimates,WHO 2013)<sup>1</sup>. The incidence in India is also alarming, The National Cancer Registry has reported, a rate of 25 to 30 per 100,000 women per year in cities like Bombay and Delhi. Earlier breast cancer was less common

and was seen in 65 to 70% of patients above 50 years of age in Pune city. Only 30 to 35% women were below fifty years of age. Breast cancer accounts for 31.3% of all cancers in women in Pune. There is an alarming rise in 30 to 40 years of age group<sup>2</sup>. According to many studies breast cancer in younger age groups tends to be more advanced and more aggressive than older age groups<sup>3</sup>. Cancer cells may have or may not have receptors for hormones e.g. the breast cancer cells

may have either receptor for oestrogen hormone or for progesterone hormones. Depending on the sensitivity of the receptor to specific hormones the cancer may be called **estrogen-receptor-positive** (ER +) or progesterone –receptor-positive (PR +). These receptors may promote growth of the cancer cells. Roughly two out of every three breast cancers test positive for hormone receptors<sup>4</sup>. Receptor sensitivity testing is important in the management of breast cancer. The physician can decide whether the management of breast cancer is hormone dependent or with any other treatment.

### Selection of patients:

A retrospective study of 37 breast cancer patients from Pune city, ranging from 30 to 70 yrs of age was included. The patients had undergone unilateral breast cancer treatment by modified radical mastectomy with axillary dissection from April 2009-March 2011. All types of histologically confirmed cancer cases were included.

**Method:** Following aspects were studied.

- Patient's Age.
- Histopathology report.
- Nottingham score, grading, immune-histochemistry marker.
- Estrogen, progesterone and HER - 2(Human Epidermal Growth Factor) receptor sensitivity.
- Lymph gland involvement.

### Statistical Analysis:

Data was entered in excel sheet and presented in the form of tables and graphs and subjected to Chi square test. It was further analyzed using SPSS software system (version 20). Probability (P) < 0.05 was considered as significant. As the study was retrospective one, the IRB approval was not required. It was in accordance with rules and regulations of Institutional Ethics Committee.

### OBSERVATION AND RESULT:

The patients were divided into two age groups: <40 years and >40 years. Mean age of diagnosis in

the younger women was 37.3 yrs (range 30 to 40 yrs) and mean age of diagnosis was 53.2 yrs in the higher age groups (range 41 to 70 yrs).

### DISCUSSION:

In the present study 10 patients were less than 40 yrs of age ( 27.8%) and 26 patients were more than 40 yrs of age (72.2%). Age was not available for one patient. Breast cancer risk increases with age. Late diagnosis may also be responsible for higher prevalence in women above 40 yrs of age. It is reported that, in Iran about 17% patients are less than 40 yrs of age. Mean age at diagnosis was 48.78 yrs (63 yrs in U.S.A., around 51 yrs in Iran). Progesterone receptor status (P.R.S.) was not statistically significantly different between less than 40 yrs and more than 40 yrs of age .(p = 0.518) (Table and graph no. 2a, 2b). The majority of tumors in younger women had positive progesterone receptor and higher stage in Iran<sup>5</sup>. There is a relation between all of these features and more aggressive tumors and poorer prognosis<sup>6</sup>. All of these studies support the concept that tumors developing in younger women are biologically different from tumors in older women and tend to be more aggressive with unfavorable biologic markers. Many studies from Europe and America have been reported showing that young age at diagnosis is an independent predictor of poor survival<sup>7</sup>. Table and graph no. 3a and 3b show that, age (less than 40 and more than 40) has no significant effect on estrogen receptor status (E.R.S.) (p = 0.102). Anders CK et al report that, tumors in young women have lower ER positivity. In the present study HER-2 status shows significant relation with age.

(p = 0.092) (Table 4a and graph 4b). Another analysis reported higher HER-2/epidermal growth factor receptor expression in young women. In the present study, presence of metastasis is significantly different in the two age groups. ( p = 0.097) (Table 5a and graph 5b). Lymph node involvement was not significantly different in the two age groups. ( p = 0.260)(Table and graph 6a

and 6b). Winstanley et al<sup>8</sup> have not found a significant association between estrogen or progesterone receptor and lymph node status, as was also found in the present study. ( $p = 0.164$ ) (Table 7a and graph 7b). The difference in Nottingham score for the two age groups was not significant. ( $p = 0.178$ ) (Table 8a and graph 8b) Distribution of patients according to age and grade of cancer revealed a statistically significant difference ( $p < 0.05$ ) in grade two and three. (Table 9a and graph 9b). Some studies have revealed higher tumor grades in younger women as compared to older women<sup>9,10,11</sup>. Most of the patients had Duct cell carcinoma (80.5%), while remaining had other different types of breast cancer. The most common histological finding was invasive ductal carcinoma, involving 92 patients (87.6%), in Iran. In the present study, Paget's disease was also present in three patients.

Hormonal receptor status indicators (Table 10 a and figure 10b) reveal the following:

Group V had 13 patients with (ER -ve, PR -ve, HER 2 NEU +ve)

Triple negativity status (ER-ve, PR-ve, HER 2 NEU -ve) was seen in 7 patients in Group I.

Group III: (ER +ve, PR +ve, HER 2 NEU -ve) and Group IV: (ER +ve, PR -ve, HER 2 NEU +ve) represented 5 patients each.

Triple positivity status (ER,PR, HER 2 NEU +ve) was seen in 4 patients in Group II.

Less than three patients were seen in

Group VI: (ER -ve, PR +ve, HER 2 NEU +ve),

Group VII: (ER +ve, PR -ve, HER 2 NEU -ve) and

Group VIII: (ER -ve, PR +ve, HER 2 NEU -ve)

It is observed that, in the patients studied in Pune, 25 were PR -ve (69.4%) and 20 patients (55.6%) were ER -ve and PR -ve.

As shown in the pie diagram (Figure 10b), maximum number of patients had the combination ER -ve, PR -ve and HER-2 NEU +ve.

## CONCLUSION:-

Retrospective analysis of breast cancer patients revealed the pattern of Nottingham's score,

grading, immunohistochemistry marker study including ER, PR and HER2Neu sensitivity. This indicated a general preponderance of ER -ve, PR -ve patients in the population of Pune. The above data provides a baseline strategy for planning a module of sustainable integrative model for management of breast cancer. Thus the treatment has to be customized, taking into consideration the disease features and findings of Pune population.

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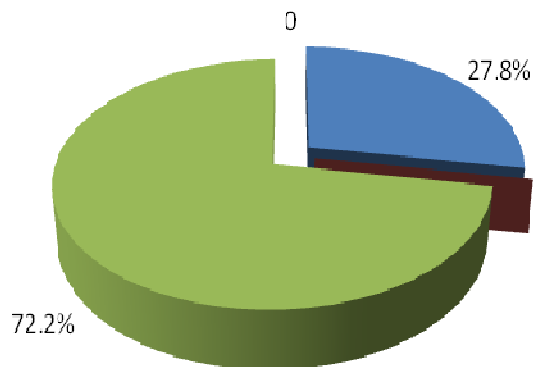
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### Tables and Figures:

**Table 1: a) Age Distribution of Studied Patients**

AGE < 40 YRS		AGE > 40 YRS		TOTAL	
NO.	%	NO.	%	NO.	%
10	27.8	26	72.2	36	100

**Figure 1: b) Age Distribution of Studied Patients**

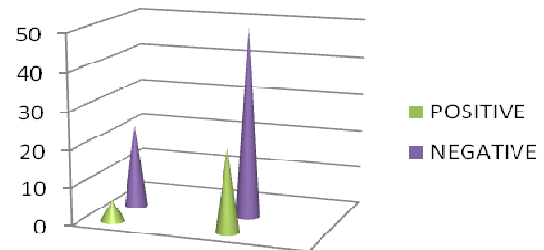


**Table 2: a) Distribution of Progesterone Receptor Status**

Progesterone Receptor Status	AGE < 40 YRS		AGE > 40 YRS		Total
	NO.	%	NO.	%	
POSITIVE	2	5.6	8	22.2	10
NEGATIVE	8	22.2	18	50	26
TOTAL	10	27.8	26	72.2	36

Chi square= 0.418 df = 1 p = 0.518 ( the difference is not statistically significant)

**Figure 2: b) Distribution of Progesterone Receptor Status**

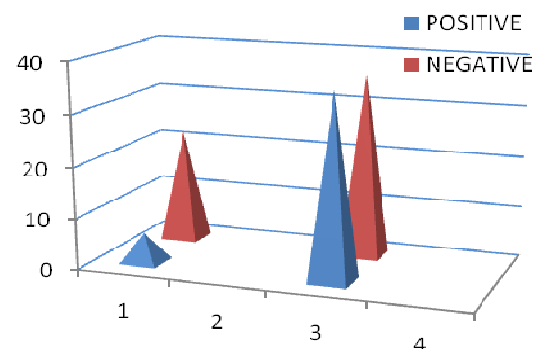


**Table 3: a) Distribution of Estrogen Receptor Status**

Estrogen Receptor Status	AGE < 40 YRS		AGE > 40 YRS		Total
	NO.	%	NO.	%	
POSITIVE	2	5.6	13	36.1	15
NEGATIVE	8	22.2	13	36.1	21
TOTAL	10	27.8	26	72.2	36

Chi square= 2.67 df = 1 p = 0.102 ( the difference is not statistically significant)

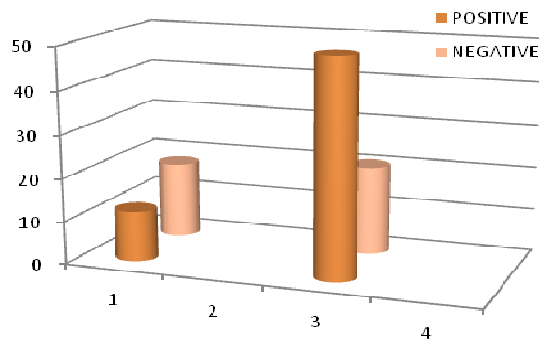
**Figure 3: b) Distribution of Estrogen Receptor Status**



**Table 4: a) Distribution of HER-2 Status**

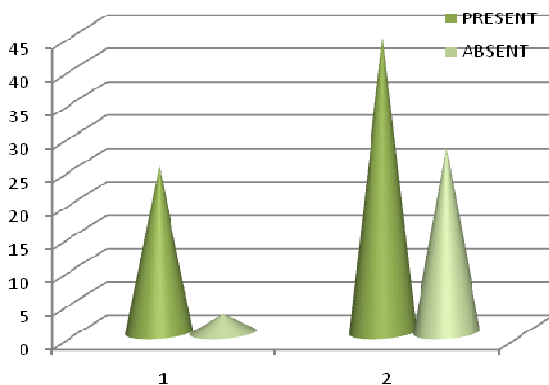
HER-2 Status	AGE < 40 YRS		AGE > 40 YRS		TOTAL
	NO.	%	NO.	%	
POSITIVE	4	11.7	17	50	21
NEGATIVE	6	17.7	7	20.6	13
TOTAL	10	29.4	24	70.6	34

Chi square= 2.84 df = 1 p = 0.092 ( the difference is statistically highly significant)

**Figure 4: b) Distribution of HER-2 Status**

**Table 5: a) Distribution of Presence of Metastasis**

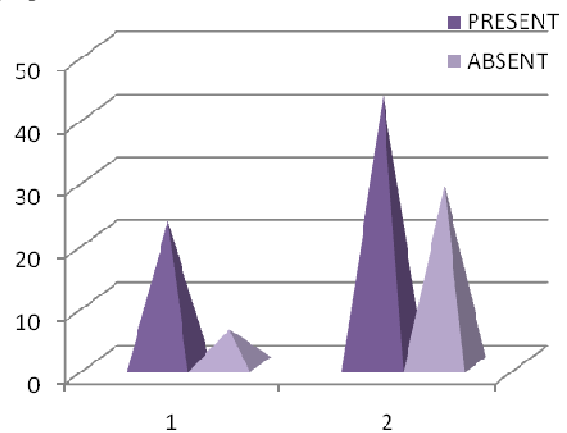
METASTASIS	AGE < 40 YRS		AGE > 40 YRS		TOTAL
	NO.	%	NO.	%	
PRESENT	9	25	16	44.4	25
ABSENT	1	2.8	10	27.8	11
TOTAL	10	27.8	26	72.2	36

Chi square= 2.76 df = 1 p = 0.097 ( the difference is statistically highly significant)

**Figure 5: b) Distribution of Presence of Metastasis**

**Table 6: a) Distribution of Patients According to Lymph Nodes Involvement.**

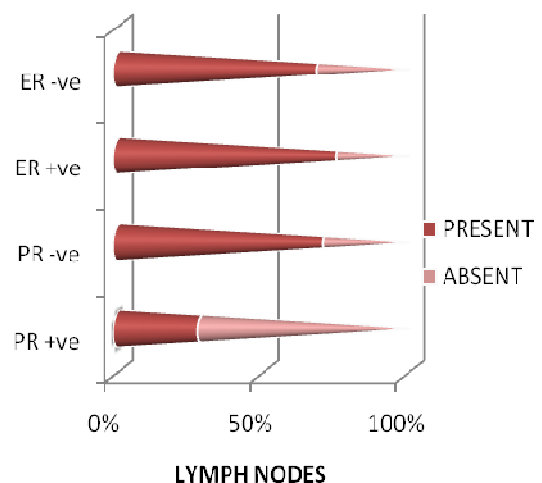
LYMPH NODES	AGE < 40 YRS		AGE > 40 YRS		TOTAL
	NO.	%	NO.	%	
PRESENT	8	22.9	15	42.9	25
ABSENT	2	5.7	10	28.6	11
TOTAL	10	28.6	25	71.4	35

Chi square= 1.27 df = 1 p = 0.260 ( the difference is not statistically significant)

**Figure 6: b) Distribution of Patients According to Lymph Nodes Involvement**

**Table 7: a) Distribution of Patients according to Lymph Nodes Involvement and Hormone Receptivity**

LYMPH NODES INVOLVEMENT				
	Present	Absent	Total	
	NO.	NO.	NO.	%
PR +ve	2	5	7	11.3
PR -ve	17	7	24	38.7
ER +ve	9	3	12	19.4
ER -ve	13	6	19	30.6
TOTAL	41	21	62	100

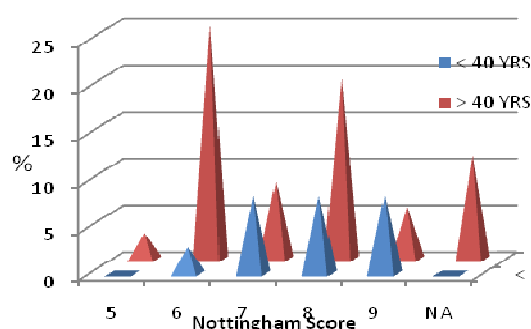
Chi square= 5.11 df = 3 p = 0.164 ( the difference is not statistically significant)

**Figure 7: b) Distribution of Patients according to Lymph Nodes Involvement and Hormone Receptivity**


**Table 8: a)** Distribution of Patients according to Nottingham score

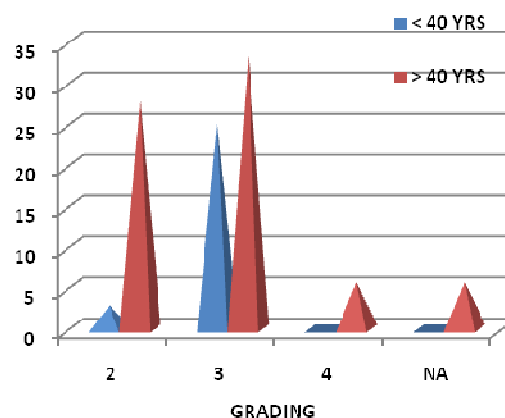
Nottingham Score	AGE < 40 YRS		AGE > 40 YRS		Total
	NO.	%	NO.	%	
5	0	0	1	2.8	1
6	1	2.8	9	25	10
7	3	8.3	3	8.3	6
8	3	8.3	7	19.4	10
9	3	8.3	2	5.6	5
NA	0	0	4	11.1	4
TOTAL	10	27.8	26	72.2	36

Chi square= 4.92 df = 3 p = 0.178 ( the difference is not statistically significant)

**Figure 8: b)** Distribution of Patients according to Nottingham score**Table 9: a)** Distribution of Patients according to Age and Grading

Grading	Age < 40 YRS		Age > 40 YRS		Total
	NO.	%	NO.	%	
2	1	2.8	10	28	11
3	9	25	12	33	21
4	0	0	2	5.6	2
NA	0	0	2	5.6	2
TOTAL	10	28	26	72	36

Chi square= 3.83 df = 1( Grade 2 & 3) p < 0.05 ( the difference is statistically significant)

**Figure 9: b)** Distribution of Patients according to Age and Grading**Table 10: a)** Hormone receptor status:

Group I: Triple negativity status(ER,PR, HER 2 NEU – ve)

Sr. No	Age (Yrs)	ER receptor	PR receptor	HER 2 NEU receptor
1	55	-ve	-ve	-ve
2	55	-ve	-ve	-ve
3	40	-ve	-ve	-ve
4	40	-ve	-ve	-ve
5	37	-ve	-ve	-ve
6	45	-ve	-ve	-ve
7	40	-ve	-ve	-ve

Group II: Triple positivity status(ER,PR, HER 2 NEU +ve)

Sr.No	Age(Yrs)	ER receptor	PR receptor	HER 2 NEU receptor
1	50	+ ve	+ ve	+ ve
2	50	+ ve	+ ve	+ ve
3	55	+ ve	+ ve	+ ve
4	50	+ ve	+ ve	+ ve

Group III:ER +ve, PR +ve, HER 2 NEU –ve

Sr. No	Age (Yrs)	ER receptor +ve	PR receptor +ve	HER 2 NEU receptor -ve
1	35	80%	90%	-ve
2	35	80%	90%	-ve
3	45	40%	50%	-ve
4	45	80%	80%	-ve
5	42	70%	30%	-ve

Group IV:ER +ve , PR –ve,  
HER 2 NEU +ve

Sr.No	Age(Yrs)	ER receptor +ve	PR receptor -ve	HER 2 NEU receptor +ve
1	58	80%	-ve	+
2	70	50%	-ve	+++
3	50	50%	-ve	+++
4	30	30%	-ve	+++
5	45	45%	-ve	+++

Group V: ER –ve,PR –ve,HER 2 NEU +ve

Sr. No	Age (Yrs)	ER receptor -ve	PR receptor -ve	HER 2 NEU receptor +ve
1	46	-ve	-ve	+
2	64	-ve	-ve	++
3	38	-ve	-ve	+++
4	40	-ve	-ve	+++
5	50	-ve	-ve	+++
6	55	-ve	-ve	+++
7	50	-ve	-ve	+++
8	65	-ve	-ve	+++
9	45	-ve	-ve	+++
10	40	-ve	-ve	+++
11	65	-ve	-ve	+++
12	32	-ve	-ve	++
13	60	-ve	-ve	+++

Group VI:ER –ve,PR +ve,HER 2 NEU +ve

Sr.No	Age(Yrs)	ER receptor -ve	PR receptor +ve	HER 2 NEU receptor +ve
1	50	-ve	20%	+

Group VII: ER +ve, PR -ve, HER 2 NEU -ve

Sr. No	Age (Yrs)	ER receptor +ve	PR receptor -ve	HER 2 NEU receptor -ve
1	45	20%	-ve	-ve
2	63	95%	-ve	-ve

Group VIII:ER -ve,PR +ve,HER 2 NEU -ve

Sr. No	Age (Yrs)	ER receptor -ve	PR receptor +ve	HER 2 NEU receptor -ve
1	33	-ve	10%	-ve

Figure No. 10 b) Hormone Receptor Status

