



IMMUNO HISTO CHEMISTRY PROFILE OF BREAST CANCER- RETROSPECTIVE ANALYSIS FROM A TERTIARY CENTER IN INDIA

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ABSTRACT

Introduction: Breast cancer is the most common cancer among women in India and globally and the leading cause of cancer mortality among females. Early stage breast cancer (>60%) is common in the western population with 72.7% Luminal A sub type, 12.2% TNBC, 15-25% HER2 positive and 12% unknown status. In India, the locally advanced breast cancer (LABC) constitutes 50 to 60% of the patients presenting for treatment and 6–25% have metastases with 51.2% Luminal A and Luminal B subtype, 16.7% HER2neu positive and 29.8% triple negative. The 5 year disease free survival (DFS) rate of 70% and overall survival rate of 78% for early breast cancer.

Materials and methods: All cases of breast cancer who were treated in the Department of Medical Oncology, Madurai from January 2017 to December 2020 were included in the study. Out of 400 patients 323 breast cancer patients were analysed for Immuno Histo Chemistry.

Results: Among 323 patients, 54.79% has hormonal receptor positivity, 19.50% triple negative, 25.69% HER2 enriched.

Discussion: Prevalence of TNBC in India is considerably higher compared with Western populations as suggested by various meta-analysis studies with Indian trial having 51.2% HR positive tumours, HER2 positive tumours in 16.7% and TNBC in 29.8%. In our study, 54.79% has hormonal receptor positivity, 19.50% triple negative, 25.69% HER2 enriched.

Conclusion: The breast cancer is the most common cancer and the leading cause of cancer mortality among females. In our study we found that higher percentage of TNBC compared to western countries.

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INTRODUCTION

Breast cancer has ranked number one cancer among Indian females with age adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women. Data reports from various latest national cancer registries were compared for incidence, mortality rates. The age adjusted incidence rate of carcinoma of the breast was found as high as 41 per 100,000 women for Delhi, followed by Chennai (37.9), Bangalore (34.4) and Thiruvananthapuram District (33.7)¹.

In 2018, 2.1 million women globally were diagnosed to have breast cancer and this is the most common cancer among women in India and globally. It is also the leading cause of cancer mortality among females. Genetic predisposition accounts for 5-10% of breast cancer. In India the incidence of breast cancer is in rising trends due to changes in reproductive risk factors, dietary habits and lifestyle changes².

A study from north India in women has reported a strong association of risk factors like breast-feeding, location (urban/rural) and increased BMI with breast cancer³. Increased breastfeeding and physical activity were protective for both ER+ and ER- breast cancer⁴.

Lifetime duration of breastfeeding was inversely associated with breast cancer risk among premenopausal women⁵. Living in rural areas decreases the risk for breast carcinoma as compared to urban counterparts mainly due their adherence to rural lifestyle⁶.

According to globacon 2020, female breast cancer has surpassed lung cancer as the most commonly diagnosed cancer. Female breast cancer constitutes 11.7% of all cancers and ranks fourth in mortality constituting 6.9% of all sites⁷.

The peak incidence of breast cancer occurs between 60-64 years in western countries but in Indian women it is between 45-49years⁸. Early stage breast cancer (>60%) is common in the western population with 72.7% Luminal A sub type, 12.2% TNBC, 15-25% HER2 positive and 12% unknown status^{9,10}.

Howlader *et al* reported best survival pattern among women with HR+/HER2- subtype (survival rate of 92.5% at 4 years), followed by HR+/HER2+ (90.3%), HR-/HER2+ (82.7%), and finally worst survival for triple-negative subtype (77.0%)¹¹.

In India, the locally advanced breast cancer (LABC) constitutes 50 to 70% of the patients presenting for treatment

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which includes 6–25% having distant metastase with 51.2% Luminal A and Luminal B subtype, 16.7% HER2neu positive disease and 29.8% triple negative^{12,13}. The 5 year disease free survival (DFS) rate of 70% and overall survival rate of 78% is seen for early breast cancer¹⁴.

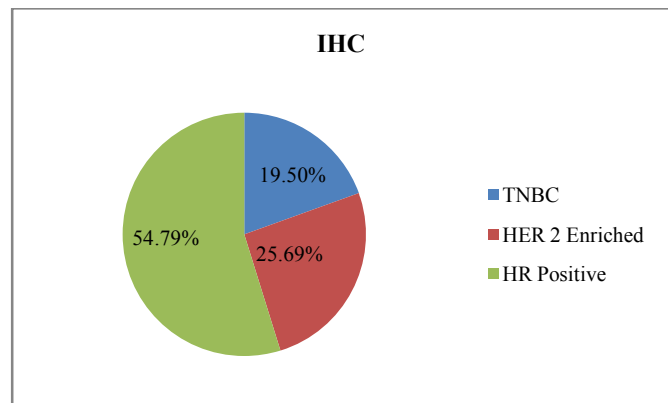
MATERIALS AND METHODS

Cases of early and locally advanced breast cancer which were treated in the Department of Medical Oncology, from January 2017 to December 2020 were included in the study. Three hundred and twenty three patients were eligible for analysis.

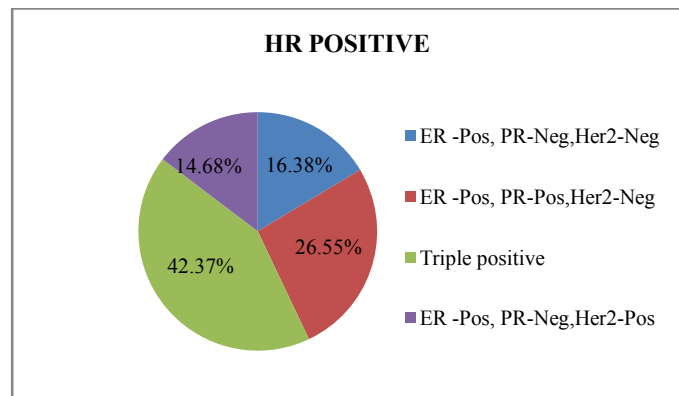
Retrospective review of all available medical records to obtain information about immuno histo chemistry was done.

RESULTS

Out of 323 patients analysed, the peak incidence occurred between 41-60 years of age (ranges between 28-82 years) with 177 patients (54.79%) having hormonal receptor positivity, 63 patients (19.50%) had triple negative and 83 patients (25.69%) had HER2 enriched subtype.

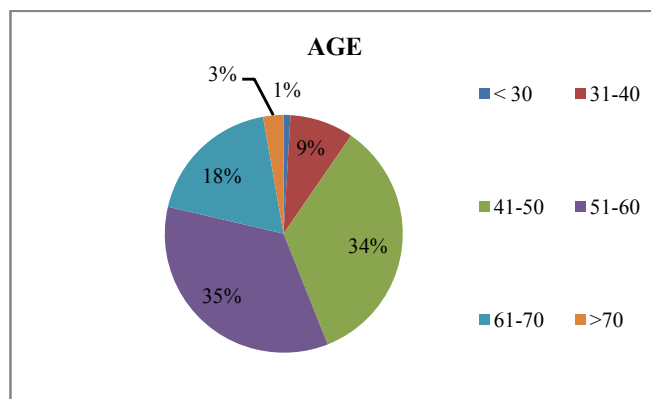


Hormone receptor positive is a heterogenous subset with differential positivity of estrogen receptor, progesterone receptor and Her2 receptor.



In this study including 323 patients, 177(54.79%) are hormone receptor positive. Out of 177 patients, 29(16.38%) had only estrogen receptor positive and negative for progesterone and her2 receptors. 47 (26.55%) had both estrogen and progesterone receptors positive and negative for her2 receptor. 75 (42.37%) had triple positive. 26 (14.68%) had estrogen receptor and her2 receptor positive and negative for progesterone receptor.

In this study in 323 patients, age ranges from 28 – 82 years , the peak incidence of breast cancer occurred between 41-60 years of age.



In this study out of 323 patients, 3(1%) are under the age of 30 years, 28 (9%) are between 31 to 40, 111 (34%) are between 41 to 50, 112 (35%) are between 51 to 60, 60(18%) are between 61 to 70, and 9 (3%) are more than 70 years.

Receptor status among patients with or under the age of 30 years

| Age | TNBC | Her2 enriched | ER+ PR- Her2 - | ER+ PR+ Her2 - | Triple positive | ER+ PR- Her2 + | Total |
|--------------------------|------|---------------|----------------|----------------|-----------------|----------------|-------|
| Less than or equal to 30 | 1 | 0 | 0 | 0 | 2 | 0 | 3 |

Receptor status among patients with 31 - 40 years of age

| Age | TNBC | Her2 enriched | ER+ PR- Her2 - | ER+ PR+ Her2 - | Triple positive | ER+ PR- Her2 + | Total |
|-------|------|---------------|----------------|----------------|-----------------|----------------|-------|
| 31-40 | 5 | 8 | 2 | 3 | 9 | 1 | 28 |

Receptor status among patients with 41 - 50 years of age

| Age | TNBC | Her2 enriched | ER+ PR- Her2 - | ER+ PR+ Her2 - | Triple positive | ER+ PR- Her2 + | Total |
|-------|------|---------------|----------------|----------------|-----------------|----------------|-------|
| 41-50 | 19 | 30 | 14 | 13 | 26 | 9 | 111 |

Receptor status among patients with 51 - 60 years of age

| Age | TNBC | Her2 enriched | ER+ PR- Her2 - | ER+ PR+ Her2 - | Triple positive | ER+ PR- Her2 + | Total |
|-------|------|---------------|----------------|----------------|-----------------|----------------|-------|
| 51-60 | 24 | 28 | 9 | 18 | 24 | 9 | 112 |

Receptor status among patients with 61 - 70 years of age

| Age | TNBC | Her2 enriched | ER+ PR- Her2 - | ER+ PR+ Her2 - | Triple positive | ER+ PR- Her2 + | Total |
|-------|------|---------------|----------------|----------------|-----------------|----------------|-------|
| 61-70 | 12 | 16 | 3 | 10 | 13 | 6 | 60 |

Receptor status among patients with more than 70 years of age

| Age | TNBC | Her2 enriched | ER+ PR- Her2 - | ER+ PR+ Her2 - | Triple positive | ER+ PR- Her2 + | Total |
|--------------|------|---------------|----------------|----------------|-----------------|----------------|-------|
| More than 70 | 2 | 1 | 1 | 3 | 1 | 1 | 9 |

DISCUSSION

The aim of this retrospective analysis was to study the immuno histo chemistry profile of breast cancer patients who were treated from January 2017 to December 2020 at a tertiary care center in India.

The incidence of breast cancer is increasing rapidly in Asian countries and being the most frequently diagnosed cancer and the leading cause of cancer death in women¹⁵.

According to globacon 2020, female breast cancer has surpassed lung cancer as the most commonly diagnosed cancer constituting 11.7% of all cancers and ranks fifth in mortality constituting 6.9% of all sites. The breast cancer is the most frequently diagnosed cancer in the vast majority of the countries (154 of 185) and is also the leading cause of cancer death in over 100 countries. In India breast cancer in females constitutes 14% of all cancers with mortality of 12.1%^{7,16}.

Leong *et al* reported the incidence of early breast cancer in western countries ranging from 60% to 70% and the remaining being advanced breast cancers¹⁷.

Women with breast cancer in India are detected clinically in contrast to western countries where most breast cancers are detected by screening. Up to two-thirds of patients present with local invasion with one-third being with skin and/or chest wall involvement (T4a-c) and 6–25% present with metastases¹².

In this study breast cancer age distribution peaks between 41-60 years. The median age of patients is approximately a decade younger than the West¹⁸. This is likely to be due to the different age distribution of the Indian population, where only 7% of the population is above the age of 60 years¹⁹.

The proportion of tumors with various patterns of receptor expression is reported in the Western literature^{20,21}. Nadia *et al* reported US incidence of breast cancer subtypes as Luminal A 72.7%, Luminal B 10.3%, and TNBC 12.2%, HER2 positive 15-25% and 12% unknown status⁹. Saber Fallahpour *et al* reported as luminal A subtype was the most commonly diagnosed, accounting for 59.0% of all cases, with a rate of 103.3 per 100 000, followed by triple-negative (15.1 per 100 000), luminal B (13.5 per 100 000) and HER2-enriched (7.0 per 100 000) with survival differed significantly between each molecular subtype, with patients with the luminal A subtype experiencing the longest survival, followed by those with the luminal B and HER2-enriched subtypes. The poorest survival was observed among patients with the triple-negative subtype²².

Mustapha Abubakar reported, 34% were luminal A-like, 33% were luminal B-like, 13% were HER2-enriched, and 20% were triple-negative, respectively with overall, all-cause mortality and recurrence differed significantly by tumor subtype. In general, women with luminal A-like tumors had better survival outcomes than those with the other subtypes²³.

A tertiary care centre in south India has recently reported a high percentage of triple negativity (25%) in their breast cancer patients (compared to the West) and a similar percentage of patients (27%) with HER2 positivity²⁴.

Prevalence of TNBC in India is considerably higher compared with that seen in Western populations as suggested by various meta-analysis studies. Trial from India showed 51.2% HR positive tumours, HER2 positive tumours in 16.7% and TNBC in 29.8%¹³.

In this study, 54.79% patients had hormonal positivity, 19.50% had triple negative, 25.69% had HER2 enriched status. The overall receptor expression pattern of patients in this study suggests a lower fraction of endocrine receptor-positive, higher fraction of triple negative and similar fraction of HER2-positive disease compared to the Western data.

As reported by TMH India, this study also found a lower proportion of Indian breast cancer patients have hormone receptor positive and a higher fraction have triple negative phenotype compared to Western populations. These differences could, at least partly, be explained by the lower average age of our patients.

CONCLUSION

Breast cancer is the most common cancer and the leading cause of cancer mortality among females. In this study, most of the patients presented a decade earlier with higher percentage of TNBC and HER2 positive disease compared to western countries.

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Declarations

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Conflict of interest: none

Ethical approval: none

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