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Original Research Article

High prevalance of triple negative markers in breast cancer patients in North Maharashtra

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ABSTRACT

Breast cancer is the most prevalent cancer among women worldwide. The Bloom Richardson grading has been applied to most breast cancers. There are different biologic subtypes of breast cancer according to immunohistochemistry (IHC). Clinically, these subtypes are characterized on the basis of expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). Among them, Triple Negative Breast Cancer (TNBC) which lacks expression of the ER, PR, and HER-2-neu, is most aggressive form. TNBC cases have worse prognosis, require aggressive chemotherapy and are difficult to manage. The advent of neoadjuvant chemotherapy has highlighted the importance of IHC, Breast Ca and TNBC. The aim and objective of this study is to find prevalence of TNBC in Breast Cancer patients in North Maharashtra. This is a 3- Year ambiceptive analysis done to study the incidence of TNBC among Breast Cancer cases. Out of 58 Breast Cancer cases diagnosed in our institute, 30 cases in which IHC was done were included in this study. Postmortem breast cancer cases, core needle biopsies and mastectomies in which IHC was not done were excluded. Among 30 cases studied, 53.33% cases were TNBC, 23.33% cases were ER and PR positive, 10% cases were only HER-2-neu positive, 6.66% cases were only ER positive, 3.33% cases were only PR positive, and 3.33% cases were all three ER, PR and HER-2 neu positive. To conclude, India has considerably higher prevalence of TNBC, as compared to the Western countries. This finding has significant clinical relevance as it may have contributed to poor outcomes in patients with breast cancer in India. With advent of neoadjuvant chemotherapy, use of Modified Bloom- Richardson Grading & IHC is of crucial importance. To understand the determinants of TNBC in India additional research is needed for diagnosis and treatment follow-up.

1. Introduction

The most prevalent cancer among women in urban India is breast cancer,[1] which accounts for 21% of all malignancies globally. It is a heterogeneous disease with numerous biological subgroups that can be identified using a DNA microarray examination of gene expression.[2] Markers of prognosis in breast carcinoma depend on tumor size, tumor TNM stage, lymphatic & vascular invasion and number of positive axillary nodes. Histological tumor types with proliferative indices, steroid hormone receptors remain the important parameter to assess the treatment outcomes. There are different subtypes of breast cancer according to immunohistochemistry, among them Triple-Negative Breast Cancer (TNBC) is the most aggressive form. Triple-negative breast cancer is called so, because it lacks expression of the estrogen receptor, progesterone receptor, and HER-2-neu.

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ER/PR/Her-2-neu Positive	Triple negative Breast Cancer
Tend to present with less aggressive clinical features.	Tend to present with more aggressive clinical features.
Effectively and routinely treated with respective targeted therapy.	Tend to recur earlier with higher frequency.
	TNBCs lack targeted therapy and are treated with systemic chemotherapy drugs.

It is well recognised that these biological subgroups have a variety of clinicopathological and molecular characteristics with prognostic and therapeutic consequences.[3] The standard management of breast cancer currently includes hormone receptor analysis, however in India, affordability and the cost of the evaluation are the two main obstacles to implement hormone receptor analysis. Given the lack of information on hormone receptors and the rising prevalence of aggressive tumors and locally advanced breast cancer (LABC), it makes sense to assess the hormonal state of breast cancer in India. Triple negative breast cancer (TNBC) is a relatively new idea and a popular area of study. Additionally, it has a shorter disease-free survival rate and is linked to aggressive tumors that are more common in younger age groups. The current study aims to assess the hormone receptor status of patients arriving at a tertiary care facility in North Maharashtra, as well as the prevalence of TNBC, its clinical and biological characteristics, and how these patients fare as compare to those who do not have TNBC.

2. Aims and Objective of the Study

To find prevalence of Triple Negative Breast Cancer in Breast Cancer patients in North Maharashtra.

3. Material and Methods

This is a 3- Year ambiceptive analysis done to study the incidence of TNBC among Breast Cancer cases diagnosed in our institute. A data of total of 58 breast cancer cases were analyzed by histopathology and 28 cases in which IHC was not done were excluded & in which IHC evaluation was performed were included in this study. However, Postmortem breast cancer cases, core needle biopsies and mastectomies in which IHC was not done were excluded.

All the specimens were fixed in 10% Neutral buffered formalin, then processed into paraffin embedded sections and were stained with haematoxylin & eosin and Imunohistochemistry (IHC) comprising of ER, PR & Her-2-neu was done in all 30 cases.

4. Results

Breast carcinoma prognostic evaluation showed–

There were a total 58 breast carcinoma patients diagnosed at our institute during the study period. IHC could not be done in 28 cases due to various problems, which were excluded from study.

In patients in which IHC was done, according to Histopathological Grading (Modified Scarff-Bloom-Richardson Grading), in Grade I & II, patients with TNBC are almost in equal proportion with patients having any of ER, PR or Her-2 positive. While TNBC are found to be more in Grade III.

There were 60% patients with TNBC having age less than 50 years. Mean age at diagnosis of TNBC was 45 years while of non- TNBCs was 51 years.

Tumor size of 81.25% TNBCs was found to be more than 5 cms and 78.57% other carcinomas was found to be less than 5 cms.

Among 30 cases studied, 53.33% cases were TNBC, 23.33% cases were ER and PR positive, 10% cases were only HER-2-neu positive, 6.66% cases were only ER positive, 3.33% cases were only PR positive, and 3.33% cases were all three ER, PR and HER-2 neu positive.

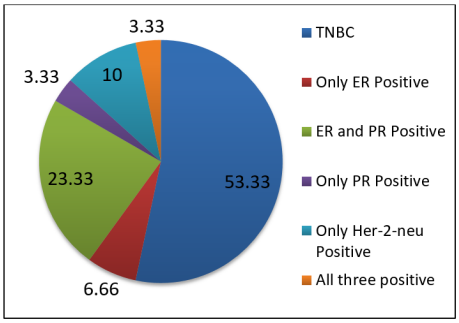

Fig. 1: Distribution according to IHC

5. Discussion

Breast cancer is becoming more prevalent worldwide and it is a significant subject of research and worry for medical professionals in India. Due to the scarcity of data from India and the high frequency of LABC, the introduction of modern technology tools providing insights into tumor biology is another crucial field of research.[3]The present study is a retrospective evaluation of the presence of triple negative breast cancer by IHC in North Maharashtra population.

Prevalence of TNBC in India ranged from 27% to 35% across studies, with a summary estimate of 31%.[4] The prevalence of TNBC in our study population was found to be 53.33%. As per the available literature, higher prevalence of TNBC is observed in the Indian population than in Western populations.[4] However, the prevalence rates reported by various Indian studies showed considerable variation among different regions of the country.

Table 1: Total no. of patients studied

Grades according to Modified Scarff-Bloom-Richardson histologic grading	Patients in which IHC was done	Patients in which IHC was not done
Grade I	10	10
Grade II	11	12
Grade III	09	06
Total	30	28

Table 2: Distribution according to histopathological grades

Grades according to Modified Scarff-Bloom-Richardson histologic grading	TNBC	ER/ PR/ HER-2 positive breast carcinomas
Grade I	4	6
Grade II	6	5
Grade III	6	3
Total	16	14

Table 3: Distribution according to age

Age	TNBC	Other Carcinomas
< 40 years	01	01
40-50 years	08	06
> 50 years	07	06
Total	16	14

Table 4: Distribution according to tumor size

Tumor Size	TNBC	Other Carcinomas
< 5 cms	03	11
> 5 cms	13	03
Total	16	14

Table 5: Comparison with other studies

Study	Ambroise et al (2011)	Saha et al (2012)	Krishnamurthy et al (2012)	Rao et al (2013)	Zubeda et al (2013)	Sharma et al (2014)	Patnayak et al (2015)	Akhtar et al (2015)	Present Study (2022)
Mean age at diagnosis	53.8 years	48.8 years	46.6 years	-	50 years	46.1 years	50.7 years	48.25 years	45 years
Tumor Size	>5 cms- 7.8%	>5cms- 33.36%	-	>5cms- 19.8%	-	>5 cms- 24.8%	>5 cms- 10.9%	>5 cms- 83.78%	TNBC – >5 cm- 81.25% Non-TNBC- >5 cm-21.4%
Histological Grading	Grade III- 33.3%	-	Grade III- TNBC- 96%	Grade III- 15.9%	-	Grade III- 63%	Grade III- 35.2%	Grade III- 64.86%	Grade III- TNBC- 37.5% Non-TNBC- 21.42%
TNBC (%)	25.5%	30.4%	18.5%	50%	46%	31.9%	22.7%	43.7%	53.33%

The prevalence of TNBC in our study was 53.33%, which is comparable with the studies of Rao et al. (50%),[5] Zubeda et al. (46%),[6] Sharma et al. (31.9%),[7] Saha et al. (30.4%),[8] Ambroise et al (25.5%),[9] Patnayak et al.(22.7%),[10] Krishnamurthy et al. (18.5%)[11] and Akhtar et al. (43.7%).[3] The earlier age of cancer onset, lifestyle factors like diet and obesity, reproductive factors like multiparity, socioeconomic factors, and possibly Indians' genetic susceptibility to TNBC are the factors that may have contributed to the higher prevalence of TNBC reported by studies among Indian patients.[12]

In our study, 81.25% of TNBC had tumor size more than 5cms in the greatest dimension while other 18.75% had tumor size less than 5cms.

The mean age of TNBC diagnosis in the current research was 45 years, which was in line with previously published data from India and a decade younger than that reported in the West.[9–11] The substantial disparity between the two populations' genetic, ethnic, and social makeup is probably the cause. In this study and earlier investigations, the mean ages of patients with non-TNBC upon diagnosis (52 years) did not differ in a statistically significant way.

However, this study has some limitations. The major limitations of this study are its retrospective design and small sample size. Large-scale prospective trials are required to ascertain rates of lymph node metastasis among both groups and identify a positive marker that can facilitate targeted therapy.[12] The absence of information on recurrence trends and disease-free survival is another significant restriction.

6. Conclusion

As compared to the Western countries, India has considerably higher prevalence of TNBC. This finding has significant clinical relevance as it may have contributed to poor outcomes in patients with breast cancer in India. Various risk factors, largely related to lifestyle, socioeconomic status, obesity, family history, high mitotic indices, and BRCA1 mutations, are linked to the high occurrence of TNBC in the Indian population.[13]

The molecular heterogenicity of TNBC necessitates the creation of several therapeutic modalities with various targets. Target therapies, including PARP inhibitors and CDK inhibitors, immune molecule-based treatments, such as cytokines, mAbs, ADCs, bsAbs, and neoantigen cancer vaccines, as well as OV-based treatments and ACT-based treatments, such as TIL, CAR-T, CAR-NK, CAR-M, and TCR-T, are revolutionising the therapeutic algorithm in both preclinical and clinical settings. The novel combinational treatment scenario has the potential to significantly enhance the results of patients with TNBC in addition to chemotherapy. Further investigation is necessary as immunotherapy is still in its early stages of development and faces obstacles. Basic and transnational research are both required to open up new therapeutic options for TNBC and other malignancies that are presently untreated.[14]

TNBC is arguably the most difficult subtype of breast cancer to treat and finding the best course of action for TNBC patients is still a critical unmet need in view of pre-op chemotherapy trials.

7. Source of Funding

None.

8. Conflict of Interest

None.

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