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International Journal of Molecular and Immuno Oncology

Original Article

Triple-negative breast cancer in India: Exploring age distribution and laterality patterns

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Received: 17 April 2024
Accepted: 28 August 2024
Published: 21 November 2024

DOI
10.25259/IJMIO_12_2024

Quick Response Code:

ABSTRACT

Objectives: Breast cancer is a prevailing health concern globally, with India experiencing alarming rates. This study delves into the clinicopathological features of triple-negative breast cancer (TNBC), focusing on age distribution, laterality, tumor grade, and Ki-67 expression. Understanding these parameters is essential for tailoring effective therapeutic strategies for this aggressive subtype.

Material and Methods: A retrospective analysis of 149 TNBC patients where human epidermal growth factor receptor 2 status was confirmed by fluorescent *in situ* hybridization as all the samples received are immunohistochemistry (IHC) equivocal. Clinical characteristics, including age, estrogen receptor/progesterone receptor status, Ki-67 expression, laterality, and histologic grade, were assessed through IHC. Statistical analyses, including Chi-square tests, were performed using the R language to discern differences between left and right breast cancers.

Results: TNBC constituted 30.53% of 488 breast cancer cases, with a wide range reported in Indian studies. The median age was 55 years, and age distribution significantly associated with TNBC incidence ($P < 0.001$). Left-sided TNBC predominated (69.12%), significantly influencing TNBC incidence ($P < 0.001$). Tumor grade distribution showed no significant difference between left- and right-sided TNBC. Ki-67 expression was significantly associated with TNBC ($P < 0.001$), with 96.24% exhibiting high expression (≥20%).

Conclusion: This study provides a detailed analysis of TNBC clinicopathological characteristics, revealing significant associations in age distribution, laterality, and Ki-67 expression. The observed left-sided predominance and the association with Ki-67 underscore the need for vigilant monitoring and personalized treatment strategies in TNBC patients. The findings contribute to understanding TNBC heterogeneity, paving the way for tailored therapeutic approaches and emphasizing the importance of continued research in this complex disease.

Keywords: Triple-negative breast cancer, Breast cancer, Laterality, Age distribution, Ki67, Left-to-right ratio

INTRODUCTION

Breast cancer stands as one of the prevalent forms of cancer globally, and India is no exception to this alarming trend. It is a heterogeneous disease that holds the top spot in cancer incidence among Indian women, carrying a cumulative risk of 2.81. According to Globocan Data 2020, breast cancer cases in India contribute to 13.5% of all cases and account for 10.6% of related deaths.[1]

This complex disease manifests with diverse biological subtypes, each exhibiting distinct clinicopathologic and molecular characteristics, impacting prognostic and predictive outcomes.[2] The classification of breast cancer into luminal A, luminal B, basal-like, human epidermal growth factor receptor 2 (HER2)-positive, and normal-like subtypes underscores its molecular diversity.

Of notable concern is the aggressive nature of triple-negative breast cancer (TNBC), a subtype that lacks expression of estrogen receptor (ER), progesterone receptor (PR), and HER2.

TNBC incidences reported as high as 31% in several parts of India[2,3] pose challenges in treatment due to its unresponsiveness to hormonal- or trastuzumab-based therapies. The prognosis for TNBC remains notably severe, with higher recurrence risks and poorer overall survival compared to other subtypes,[4] particularly affecting younger[5] and premenopausal women,[2] as well as those of African-American[6] and Asian descent.[2]

Despite significant steps in cancer treatment, a subset of patients remains vulnerable to limited responses to therapy. Current decision-making in therapy choice relies on clinical, pathological, and limited molecular factors.[4] However, the complexity of breast cancer necessitates a deeper understanding of treatment responses, considering factors such as gene mutations, cancer stage, and hormonal status.

In our study, we present a comprehensive analysis of various parameters in a cohort of 149 TNBC patients. Our study delves into age distribution, laterality, tumor grade, and the expression of Ki-67, a proliferative marker, to unravel potential associations and insights into the heterogeneity of this aggressive cancer subtype.

MATERIAL AND METHODS

Data collection

In the present study, a retrospective analysis of patients with equivocal HER2/Neu IHC status was included where their HER2 status was confirmed using the fluorescent *in situ* hybridization (FISH) technique by the cytogenetics department at SN Gene Laboratory Pvt. Ltd. FISH score of <2 was considered negative and more than 2 as positive. In total we received 488 samples of breast cancer between January 23 and November 23 from these 149 patients, which are included in this study, were TNBC cases. We analyzed the data for these patients. The clinical characteristics of the patients included were age of patients when received the samples, status for ER, PR, and Ki67, laterality, and histologic grade. Data on ER, PR, and Ki67 expression status were retrieved from the medical records of patients, which were assessed using IHC.

Informed consent was taken from patients.

Statistical analysis

The distribution of various factors was compared using the Chi-square test to determine the difference between left and right breast cancers concerning each factor. The ratio of left breast cancer to right breast cancer (left-to-right ratio [LRR]) was analyzed. The number and ratio of left- to right-sided were calculated according to different factors. All statistical analyses were performed using the R language. $P < 0.05$ was considered statistically significant.

RESULTS

Our study investigated the clinicopathological characteristics of triple-negative breast cancer (TNBC) in a cohort of 149 patients, focusing on age distribution, laterality, tumor grade, and Ki-67 expression. The following results show key correlations and insights [Tables 1 and 2].

Prevalence of TNBC

TNBC accounts for 30.53% out of 488 breast cancer cases observed between January and November 2023, which is consistent with reported Indian studies (11.8% to 31.9%).[5,7,8]

Age distribution

The median age of TNBC patients was 55 years, aligning with findings from Western studies reporting a median age of 53 years.[7] Patients aged 45-55 formed the largest subgroup (30.20%), showing a significant correlation with TNBC incidence (*P* value <0.001). A sharp decline in cases was seen after the age of 75 (4.69%) [Table 1]. These age-related findings are in line with previous literature by Chowdhary *et al.*[9]

Laterality

There was a significant left-sided predominance in TNBC cases, with 69.12% occurring on the left side and 30.87% on the right (*P* value <0.001) [Table 1]. The observed left-sided dominance aligns with previous studies reporting variations in breast cancer laterality.[7, 10]

Ki-67 expression

A high Ki-67 expression (>20%) was found in 96.24% of TNBC cases, indicating increased proliferative activity associated with TNBC (*P* value <0.001) [Table 1].

Tumor grade

There was no statistically significant difference in tumor grade distribution between left and right-sided TNBC cases (*P* value = 0.0943561) [Table 2].

Left vs. Right-sided TNBC

The comparison of key parameters between left and right-sided TNBC revealed no significant differences in age distribution, with the Left-to-Right Ratio (LRR) ranging from 1.50 to 6.00 across age groups (*P* value > 0.05). Both sides exhibited similarly high Ki-67 expression (>20%) (*P* value =

Table 1: Comprehensive profiling of TNBC: A 149-patient analysis.

	n	%	*P*-value
Age			
<35	4	2.60	<0.001
35–45	25	16.78	
45–55	45	30.20	
55–65	40	26.84	
65–75	28	18.79	
>75	7	4.69	
Laterality			
Left	103	69.12	<0.001
Right	46	30.87	
Grade*			
II	63	43.15	0.0979
III	83	56.84	
Ki 67**			
<20	5	3.75	<0.001
>20	128	96.24	

*Data not available for three entries, **Data not available for 16 entries. TNBC: Triple-negative breast cancer, Ki 67: Marker of proliferation.

Table 2: Comparison of the left and right TNBC: Age, grade, and Ki-67 analysis.

	Left	Right	LRR	*P*-value
Age				
<35	3	1	3.00	0.740268
35–45	15	10	1.50	
45–55	30	15	2.00	
55–65	30	10	3.00	
65–75	19	9	2.11	
>75	6	1	6.00	
Grade*				
II	38	25	1.52	0.094356
III	62	21	2.95	
Ki 67**				
<20	4	1	4.00	0.967436
>20	88	40	2.20	

*Data not available for three entries, **Data not available for 16 entries. TNBC: Triple-negative breast cancer, LRR: Left-to-right ratio Ki 67: Marker of proliferation.

0.9674364), underscoring the consistent aggressive nature of TNBC regardless of laterality [Table 2].

Data limitations

Missing data (3 entries for tumor grade and 16 for Ki-67 expression) may have influenced the overall results. Limited patient information was also a constraint in this study.

DISCUSSION

The findings of this study provide valuable insights into the demographic and clinicopathological characteristics of TNBC, contributing to a deeper understanding of this aggressive subtype of breast cancer. Several significant patterns were identified:

Age and TNBC

The age-related susceptibility of TNBC, with a peak incidence between 45-55 years and a decline after 75, is consistent with global findings and indicates a critical window for intervention in middle-aged women. This age distribution emphasizes the importance of early screening in at-risk populations.

Laterality

The observed left-sided predominance in TNBC cases may have clinical implications, particularly in understanding the biological mechanisms driving asymmetrical disease distribution. Future studies should investigate how laterality might affect treatment strategies and patient outcomes. This finding reinforces the need for vigilance in the diagnosis and management of left-sided breast cancer.

Tumor grade and Ki-67 expression

The high prevalence of grade III tumors and the elevated Ki-67 proliferation index (>20%) in TNBC reflect its aggressive nature. These findings emphasize the importance of personalized therapeutic approaches for TNBC patients, particularly those with higher tumor grades and high Ki-67 levels.

Laterality and Ki-67 expression

Despite the left-sided dominance of TNBC, no significant differences were observed between left and right-sided cases in terms of Ki-67 expression and age distribution, indicating that these factors do not appear to drive laterality differences.

Clinical implications

The study's findings underscore the need for personalized treatment strategies, especially for patients with high Ki-67 expression and advanced tumor grade. The left-sided predominance of TNBC also warrants further research to explore the underlying biological mechanisms and their potential impact on treatment responses.

CONCLUSION

This study provides a detailed analysis of demographic and clinicopathological parameters in TNBC, revealing significant associations in age distribution, laterality, and Ki-67 expression. The comparison between left- and right-sided TNBC offers additional granularity to our understanding of this complex disease, paving the way for further investigations and personalized treatment strategies in TNBC patients.

Our study has identified significant patterns in breast cancer prevalence. Our main findings indicate that breast cancer is more prevalent in the left breast among patients. Among these patients, we observed a Ki-67 proliferation index >20%, along with a higher occurrence of grade III tumors. Notably, these patterns are particularly pronounced in premenopausal women.

All the patients in our study were IHC equivocal, and their status was confirmed using FISH. In these patients, we observed a significant predominance of left-sided breast cancer with a high Ki-67 proliferation index with a higher grade. This reinforces the novel aspect of our study. These findings contribute to a better understanding of breast cancer characteristics and could inform more targeted screening and treatment strategies for at-risk populations.

Acknowledgment

The authors are thankful to the cytogenetic unit for their help.

Ethical approval

The research/study is approved by the Institutional Ethics Committee at SN Gene Laboratory Pvt. Ltd, number 116, dated 27th December 2022.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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How to cite this article: Gadhia PK, Joshi N, Vaniawala S. Triple-negative breast cancer in India: Exploring age distribution and laterality patterns. Int J Mol Immuno Oncol 2024;9:62-5. doi: 10.25259/IJMIO_12_2024