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Original Research Article

CLINICOPATHOLOGICAL CHARACTERISTICS AND TUMOUR SIZE–BASED PROGNOSTIC ASSESSMENT IN TRIPLE-NEGATIVE BREAST CANCER: A RETROSPECTIVE STUDY FROM SOUTH INDIA

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ABSTRACT

Background: Triple-negative breast cancer (TNBC) is an aggressive subtype lacking ER, PR, and HER2 expression, limiting targeted therapeutic options. Evaluation of clinicopathological and prognostic factors is essential for understanding disease behaviour. The aim and objective is to evaluate the clinicopathological characteristics of TNBC and analyse the association of tumour size with lymph node status and tumour grade.

Materials and Methods: A retrospective study of 52 TNBC cases from Tirunelveli Medical College was conducted. Formalin-fixed paraffin-embedded tissues were analysed using WHO classification and modified Bloom–Richardson grading. Immunohistochemistry was performed for ER, PR, and HER2. Statistical analysis was performed using the chi-square test, independent t-test, and one-way ANOVA, with $p < 0.05$ considered statistically significant.

Results: Most patients were aged 41–60 years (70%), with a mean tumour size of 4.20 ± 1.31 cm. Invasive ductal carcinoma NOS predominated (86%), with Grade II tumours most common (48%). Lymphovascular invasion and tumour necrosis were present in 67% and 44% of cases, respectively, while lymph node metastasis was observed in 40%. Larger tumour size was significantly associated with nodal positivity ($p = 0.005$), whereas no significant association was found between tumour size and tumour grade ($p = 0.221$).

Conclusion: TNBC predominantly presents as intermediate-grade invasive ductal carcinoma with significant association between tumour size and lymph node metastasis.

Keywords: Breast Neoplasms; Triple Negative Breast Neoplasms; Prognosis; Lymphatic Metastasis; Neoplasm Grading.

INTRODUCTION

Triple-negative breast cancer (TNBC) is a molecular subtype of breast carcinoma defined by the absence of oestrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) expression, accounting for approximately 15-20% of all breast cancers worldwide.[1] TNBC shows aggressive clinical behaviour with higher recurrence and metastasis rates compared to other subtypes.[2] The disease commonly affects younger and middle-aged women and demonstrates considerable biological heterogeneity in morphology, molecular profile, and clinical outcomes.[3]

TNBC is commonly associated with high-grade invasive ductal carcinoma and elevated proliferative activity.[4] Advances in breast cancer management have improved outcomes in hormone receptor-positive and HER2-positive cancers, whereas TNBC treatment primarily relies on chemotherapy, necessitating reliable prognostic and predictive markers.[3] Immunotherapy has shown benefit in early TNBC. Research has focused on immunohistochemical markers for prognostic stratification and therapeutic planning. In addition to

conventional histopathological parameters, features such as tumour size, histological grade, lymph node status, and lymphovascular invasion play a crucial role in determining disease behaviour and prognosis in TNBC. These parameters provide valuable insight into tumour aggressiveness, metastatic potential, and treatment response, thereby aiding in risk stratification and clinical decision-making.[5,6]

Accurate prognostic assessment in TNBC remains challenging because of its marked biological and clinical heterogeneity. Although patients share the same receptor-negative phenotype, they exhibit considerable variation in tumour morphology, disease progression, response to treatment, and survival outcomes. Consequently, evaluation of established clinicopathological parameters, including tumour size, histological grade, lymph node status, lymphovascular invasion, and associated pathological features, remains fundamental for predicting tumour behaviour, guiding therapeutic decision-making, and stratifying patient risk. Ongoing research continues to improve the understanding of TNBC heterogeneity, emphasizing the importance of integrating conventional pathological features with emerging molecular insights to optimize prognostic evaluation and patient management.[7–12]

The biological behaviour of TNBC remains unpredictable, with considerable variation in clinical outcomes even among patients with similar histopathological features. This highlights the need for improved prognostic stratification in TNBC. TNBC is characterized by a higher propensity for early recurrence, visceral metastasis, and poorer overall survival compared to other breast cancer subtypes. The absence of hormone receptors and HER2 expression limits the use of targeted therapies, making chemotherapy the mainstay of treatment. Recent advances have highlighted the role of tumour microenvironment, and immune cell infiltration in influencing tumour progression and treatment response. Emerging evidence suggests that heterogeneity within TNBC may impact prognosis and therapeutic outcomes, emphasizing the importance of comprehensive evaluation of clinicopathological parameters alongside molecular markers.[13,14]

Regional variations in patient demographics and tumour characteristics can influence the clinicopathological profile of TNBC, highlighting the need for population-specific studies. Evaluation of clinicopathological and prognostic parameters provides a more comprehensive understanding of tumour behaviour in TNBC.[13,14] Thus, the present study aimed to evaluate the clinicopathological and prognostic parameters of TNBC, and to analyse the association between tumour size and key prognostic indicators such as lymph node status and tumour grade.

Aims: To evaluate the clinicopathological and prognostic parameters of TNBC and analyse the association of tumour size with lymph node status and tumour grade.

Objectives:

1. To describe the demographic and clinicopathological characteristics of TNBC.
2. To assess the association between tumour size and lymph node status.
3. To evaluate the association between tumour size and histological tumour grade.

MATERIALS AND METHODS

This was a retrospective analytical study conducted on 52 cases of primary breast carcinoma diagnosed as TNBC in the Department of Pathology, Tirunelveli Medical College, Tirunelveli for two years, from September 2017 to September 2019.

Inclusion criteria

Cases reported as TNBC by histopathological examination (HPE) and immunohistochemistry (IHC) were included.

Exclusion criteria

Samples received after post-chemotherapy and post-radiotherapy were excluded from the study.

Methods: Archived formalin-fixed paraffin-embedded tissue blocks of 52 TNBC cases were retrieved and analysed. Clinical data including age, menopausal status, tumour size, histological type, tumour grade, tumour necrosis, lymph node status, and local tumour involvement (skin, nipple–areola, and margins) were obtained from medical records. Sections of 4–5 µm thickness were cut and stained with hematoxylin and eosin for histopathological evaluation. Tumours were classified according to WHO Classification of Breast Tumours and graded using the modified Bloom–Richardson (Nottingham) grading system.

Prognostic parameters such as tumour type, grade, necrosis, lymphovascular invasion, perineural invasion, associated DCIS component, and lymph node metastasis were assessed. IHC was performed for ER, PR, and HER2 using the DAKO EnVision method after antigen retrieval with Tris-EDTA buffer (pH 9).

Statistical Analysis: Statistical analysis was performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. The independent t-test, one-way ANOVA, and chi-square test were used as appropriate. A p-value of <0.05 was considered statistically significant.

Ethical consideration: Ethical approval for the study was obtained from the Institutional Ethics Committee of Tirunelveli Medical College, Tirunelveli prior to the commencement of the study.

RESULTS

Among 52 TNBC patients, majority were aged 51–60 years (37%), followed by 41–50 years (33%), with 15% each <40 and >60 years. Majority of patients were postmenopausal (56%) compared to premenopausal (44%) [Table 1].

Table 1: Demographic profile of TNBC patients

Parameter	Category	N (%)
Age (years)	< 40	8 (15%)
	41 – 50	17 (33%)
	51 – 60	19 (37%)
	> 60	8 (15%)
Menopausal status	Attained	29 (56%)
	Not attained	23 (44%)

The mean tumour size was 4.20 ± 1.31 cm, with 9.75 ± 4.12 lymph nodes examined and 2.64 ± 1.01 positive nodes. Most tumours were 2–5 cm (58%), with 21% each <2 cm and >5 cm. IDC NOS predominated (86%), and Grade II tumours were most frequent (48%), followed by Grade III (38%). Lymphovascular invasion and tumour necrosis were present in 67% and 44%, respectively. DCIS and perineural invasion were seen in 13% and 4%. Tumour involvement of nipple–areola, skin, and margins was noted in 4%, 8%, and 8% [Table 2].

Table 2: Clinicopathological characteristics of tumours

Parameter	Category	Value (n (%) / Mean ± SD)
General Tumour Parameters	Mean Tumour Size (cm)	4.2 ± 1.31
	Total Lymph Nodes Examined	9.75 ± 4.12
	Positive Lymph Nodes	2.64 ± 1.01
Tumour Size	< 2 cm	11 (21%)
	2–5 cm	30 (58%)
	> 5 cm	11 (21%)
Histological Type	Invasive Ductal Carcinoma (IDC NOS)	45 (86%)
	Carcinosarcoma	2 (4%)
	Medullary Carcinoma	4 (8%)
	Invasive Lobular Carcinoma	1 (2%)
Tumour Grade (Bloom–Richardson System)	Grade I	7 (14%)
	Grade II	25 (48%)
	Grade III	20 (38%)
Lymphovascular Invasion	Present	35 (67%)
	Absent	17 (33%)
DCIS Component	Present	7 (13%)
	Absent	45 (87%)
Perineural Invasion	Present	2 (4%)
	Absent	50 (96%)
Tumour Necrosis	Present	23 (44%)
	Absent	29 (56%)
Nipple & Areola	Not involved	50 (96%)
	Involved	2 (4%)
Skin	Not involved	48 (92%)
	Involved	4 (8%)
Margins	Not involved	48 (92%)
	Involved	4 (8%)

Lymph node metastasis was present in 21 (40%) and absent in 31 (60%) cases. Mean tumour size was higher in node-positive cases (5.35 ± 2.53 cm) than node-negative (3.4 ± 2.14 cm; p = 0.005). Tumour size showed a statistically significant association with lymph node metastasis, with larger tumours demonstrating higher nodal involvement (p = 0.005). No statistically significant association was observed between tumour size and tumour grade (p = 0.221) [Table 3].

Table 3: Nodal and prognostic parameters

Parameter	Category	N (%) / Mean ± SD (cm)	P-value
Lymph node metastasis	Positive	21 (40%)	—
	Negative	31 (60%)	
Tumour size vs LN status	Positive nodes	5.35 ± 2.53	0.005
	Negative nodes	3.4 ± 2.14	
Tumour size vs tumour grade	Grade I	5.57 ± 2.65	0.221
	Grade II	4.24 ± 2.66	
	Grade III	3.67 ± 2.08	

DISCUSSION

TNBC is a biologically aggressive subtype characterized by distinct clinicopathological features and adverse prognostic behaviour. In the present study, we evaluated the clinicopathological and prognostic parameters of TNBC, focusing on tumour size, histological type, grade, lymph node status, and associated pathological features, to better understand their patterns and prognostic implications. The TNBC cohort consisted predominantly of patients in the 41–60 year age group, while younger and older age groups were less represented. A higher proportion of patients were postmenopausal, indicating a predominance of TNBC in the postmenopausal age group. Similarly, Teoh et al. reported a higher mean age of 58.4 years (median 59; range 32–83 years) in their TNBC cohort, with 47 patients below the mean age and 50 patients at or above the mean age, indicating a predominance of the middle to older age group in both studies.15 This is comparable to the study by Merckx reported a median age of 51 years (range 22–85 years) in 426 TNBC patients.[16]

Similarly, Nishimura et al. reported that menopausal status may influence tumour behaviour in TNBC, with premenopausal patients often exhibiting more aggressive biological features and poorer outcomes.[17] A comparable South Indian study by Inampudi et al. reported a higher proportion of premenopausal patients (60.6%) compared to postmenopausal (39.3%), highlighting regional variation in menopausal distribution despite similar clinicopathological patterns.[18] These findings suggest that TNBC predominantly affects older, postmenopausal women, while younger premenopausal patients may show more aggressive tumour behaviour and poorer prognosis.

Most tumours in our study were invasive ductal carcinoma of no special type and commonly showed intermediate histological grade, with frequent lymphovascular invasion and a moderate proportion showing tumour necrosis, whereas DCIS component and perineural invasion were uncommon. Local involvement of the skin, nipple-areola, and margins was minimal. A comparable Indian study by Vodithala and Bhake reported a predominance of T2 tumours (63.88%), higher histological grades with Grade II (38.88%) and Grade III (58.33%), and frequent lymphovascular invasion (55.55%), along with low rates of nipple involvement (8.33%), which closely aligns with the clinicopathological patterns observed in our study.[19] Similarly, Teoh et al. reported that invasive ductal carcinoma predominated (83 cases vs 14 non-IDC), with a predominance of high-grade tumours (Grade III: 76 cases; Grade II: 19 cases; Grade I: 2 cases) and a mean tumour size of 48.3 mm (median 43.0 mm; range 10–240 mm), with most tumours measuring ≥20 mm (83 cases). Lymphovascular invasion was present in 59 cases, and absent in 38; nodal status showed 41 pN0, 28 pN1, 18 pN2, and 10 pN3; and associated DCIS was present in 44 cases and absent in 53.[15]

Similarly, a study reported by Sridevi et al., showed predominance of tumours measuring 2–5 cm (64.81%), with invasive ductal carcinoma constituting 87.04% of cases and Grade II tumours being most common (72.22%). Lymphovascular invasion was observed in 83.33% of cases. Low rates of nipple, skin, and margin involvement (5.56%).[20] These comparable findings suggest TNBC commonly presents with intermediate-sized, higher-grade tumours and frequent lymphovascular invasion, indicating aggressive disease biology, while low local involvement reflects relatively limited locoregional extension at diagnosis.

Lymph node metastasis was observed in 40% of cases, and larger tumours were significantly associated with nodal positivity, while no significant association was found between tumour size and tumour grade. A comparable pattern was reported by Astvatsaturyan et al., where nodal involvement showed variable distribution with pN0 in 82 cases, pN1 in 31 cases, pN2 in 9 cases, and pN3 in 2 cases, and the mean tumour size was 31 mm, while no significant association between tumour grade and clinicopathological parameters (MBR score III in 121 cases; $p = 0.842$), whereas AR-positive tumours were significantly larger and showed a higher incidence of axillary lymph-node metastasis.[8]

The study highlights the predominance of intermediate-grade TNBC with significant association between tumour size and nodal status.

Limitations: This study is limited by its single-centre retrospective design and relatively small sample size, which may affect the statistical power to detect weaker associations. Selection bias cannot be excluded. The absence of long-term follow-up data precluded evaluation of survival outcomes and treatment response. The findings may not be generalizable to larger or more diverse populations.

CONCLUSION

TNBC predominantly showed invasive ductal carcinoma of no special type with intermediate grade, frequent lymphovascular invasion, and tumour necrosis. Most tumours were of intermediate size with minimal local involvement. Larger tumour size was significantly associated with lymph node metastasis, supporting its association with increased nodal involvement in TNBC.

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