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Clinicopathological Profile of Carcinoma Breast and Its Association with Molecular Subtypes and Nodal Burden: A Cross-Sectional Observational Study at a Tertiary Care Hospital

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Abstract

Background: Breast cancer is the most prevalent female malignancy in India, and presentation at late stages and prevalence of triple-negative breast cancer (TNBC) are important clinical challenges. Clinical correlates of molecular subtype distribution and the burden of nodes in Indian tertiary care patients are not fully understood. Design, setting and participants: A cross sectional study was conducted in 180 women who were diagnosed with breast carcinoma in a tertiary care hospital over a period of 18 months. Age, stage, histological grade, clinical correlates, and molecular subtypes as determined by immunohistochemistry (IHC) for estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and Ki-67 were recorded. Results: The median age at diagnosis was 48 years (range 26-78); 41.1% were diagnosed with the condition before their menopause. Stage III at diagnosis in 38.3%; Stage IV in 12.2%. Molecular subtypes: Luminal A 32.2%, Luminal B 26.1%, HER2-enriched 17.8%, TNBC 23.9%. Of the patients, 58.3% had node-positive disease. Tumour size >2 cm, grade III, TNBC subtype and Ki-67 ≥ 20% were independent factors associated with nodal positivity (aOR 3.1, 2.4, and 1.7, respectively). Captions: A high proportion of the Indian breast cancer patients present with advanced stage disease. The proportion of high TNBC (23.9 %) and the high nodal positivity at diagnosis (58.3 %) in the study indicate the aggressive nature of Indian breast carcinoma. Population based screening via mammography and clinical breast examination should be given greatest emphasis.

Keywords: *Breast carcinoma; molecular subtypes; TNBC; HER2-enriched; Luminal; nodal burden; Ki-67; stage at diagnosis; India.*

Introduction

With an age-standardised incidence rate of 26.4 per 100,000 women, breast cancer is the most commonly diagnosed female cancer in India accounting for approximately 27.7% of all female cancers in the estimates of GLOBOCAN 2022 [1]. The absolute burden is enormous (226,000 new cases and 103,000 deaths due to breast cancer per year in India), and is expected to increase further due to the many contributing factors including the urbanisation, changing reproductive patterns (reduction in parity, delayed first childbirth, less breastfeeding), rising obesity, and reduced physical activity in women [2]. In the Western populations, early detection of breast cancer is commonplace, and this is achieved through population-based mammography

screening, Indian breast cancer presents at a much more advanced stage, with published tertiary care series reporting 50-70% of patients with Stage III/IV at diagnosis, versus 20-25% in the United States [3].
Immunohistochemistry (IHC) molecular subtyping (Luminal A (ER/PR+, HER2−, Ki-67 <20%) Luminal B (ER/PR+, HER2± with Ki-67 ≥20% or HER2+), HER2-enriched (ER−, PR−, HER2+) and Triple-Negative Breast Cancer (TNBC; ER−, PR−, HER2−)) offers prognostically and therapeutically actionable information in addition to histological grade and nodal status [4]. The molecular subtype is of particular clinical importance, because it occurs more frequently in younger pre-menopausal Indian women, has an aggressive biology with peak early mortality but no plateau effect in long-term survivors and is the only molecular subtype that lacks FDA/CDSCO approved targeted therapy, either hormonal or anti-HER2, making cytotoxic chemotherapy the backbone of systemic therapy [5].
Although the prognostic significance of axillary nodal burden at diagnosis has been somewhat muted in early stage breast cancer by molecular profiling, it still correlates strongly with systemic recurrence and survival, and has been the most powerful prognostic factor in breast cancer to date [6]. Knowledge of the molecular and clinicopathological parameters that predict the nodal positivity at diagnosis could be relevant for surgical management (sentinel node biopsy vs. up-front axillary clearance) and for planning adjuvant systemic therapy. This was a cross sectional study to describe the clinicopathological features, distribution of molecular subtypes and nodal burden of breast carcinoma and to find independent predictors for node positivity at a tertiary care hospital.

MATERIALS AND METHODS

2.1 Study Design and Population

Cross-sectional observational study at the general surgery/oncology outpatient and inpatient setting of a tertiary care hospital over 18 months. Inclusion: all women with histologically confirmed breast carcinoma (core-needle biopsy or excision-biopsy). Exclusion: recurrent disease (previously treated breast cancer), male breast cancer (n=2 excluded), non-epithelial tumours (lymphoma, phyllodes), bilateral synchronous cancer. IEC approved; written informed consent. STROBE guidelines.

2.2 Data Collection and IHC Classification

Structured proforma: age, menopausal status, BMI, family history of breast cancer (first-degree relative), parity, breastfeeding duration, OCP/HRT history, presenting symptom (lump/nipple discharge/pain/axillary lump/incidental), tumour size on clinical examination and imaging (USG/mammogram), AJCC 8th edition clinical stage, histological type (IDC/ILC/other), Nottingham grade, lymphovascular invasion, ER, PR (Allred score, positive ≥1/8), HER2 (IHC 0/1+/2+ with FISH confirmation for equivocal, positive = 3+ or FISH-amplified), Ki-67 (%, positive >14%, high ≥20%), axillary nodal status (clinical palpation, USG axilla, sentinel/axillary dissection histopathology). Nottingham Prognostic Index (NPI) calculated. Molecular subtype assigned per St Gallen 2023 consensus: Luminal A — ER+/PR+ (PR >20%), HER2−, Ki-67 <14%, grade I–II; Luminal B — ER+ and/or PR+, HER2+ or Ki-67 ≥20% or grade III; HER2-enriched — ER−, PR−, HER2+; TNBC — ER−, PR−, HER2−.

2.3 Statistical Analysis

SPSS v26. Descriptive statistics. Chi-square/Fisher's exact for categorical comparisons. Multivariable binary logistic regression (outcome: node-positive disease). aOR (95% CI); $p<0.05$ significant.

3. RESULTS

3.1 Clinicopathological and Molecular Profile

180 women enrolled (median age 48 years [range 26–78]; mean 49.2±11.4 years). Premenopausal: 74/180 (41.1%). Family history: 18/180 (10.0%). BMI ≥25 in 56.7%. Stage at diagnosis: I 14.4%, II 35.0%, III 38.3%, IV 12.2%. Histological type: IDC 82.2%, ILC 8.9%, mucinous 3.3%, others 5.6%. Grade: I 14.4%, II 42.2%, III 43.3%. Ki-67 ≥20% in 61.1%. Molecular subtype distribution and nodal data are in Table 1.

Table 1: Molecular Subtype Distribution and Clinicopathological Correlates (n=180)

Parameter	Luminal A (n=58)	Luminal B (n=47)	HER2-enriched (n=32)	TNBC (n=43)	p-value
Median age, years	54	48	46	44	0.002
Premenopausal, n (%)	18 (31.0%)	20 (42.6%)	16 (50.0%)	20 (46.5%)	0.11
T2 (>2cm), n (%)	26 (44.8%)	30 (63.8%)	22 (68.8%)	32 (74.4%)	0.008
Grade III, n (%)	4 (6.9%)	20 (42.6%)	18 (56.3%)	36 (83.7%)	<0.001
Ki-67 ≥20%, n (%)	0 (0%)	47 (100%)	30 (93.8%)	33 (76.7%)	<0.001
LVI, n (%)	14 (24.1%)	22 (46.8%)	18 (56.3%)	24 (55.8%)	0.003
Stage III–IV, n (%)	18 (31.0%)	28 (59.6%)	22 (68.8%)	32 (74.4%)	<0.001
Node positive, n (%)	26 (44.8%)	30 (63.8%)	24 (75.0%)	25 (58.1%)	0.023
Distant metastasis (Stage IV), n (%)	4 (6.9%)	6 (12.8%)	6 (18.8%)	6 (14.0%)	0.30

3.2 Nodal Burden and Predictors

Node-positive disease was documented in 105/180 (58.3%). Node-positive rates by subtype: Luminal A 44.8%, Luminal B 63.8%, HER2-enriched 75.0%, TNBC 58.1%. Among node-positive patients, mean positive nodes: 4.6±3.8 (range 1–22). Macrometastatic disease in ≥4 nodes (N2+ category) in 28.3% of all patients. Multivariable predictors of nodal positivity are in Table 2.

Table 2: Multivariable Logistic Regression: Independent Predictors of Node-Positive Disease (n=180)

Variable	Unadj. OR (95% CI)	p	Adj. OR (95% CI)	p
Tumour size >2 cm (T2–T4)	4.2 (2.1–8.4)	<0.001	3.1 (1.5–6.4)	0.002
Histological grade III	3.4 (1.8–6.4)	<0.001	2.4 (1.2–4.8)	0.013
TNBC subtype (vs Luminal A)	1.8 (0.9–3.6)	0.09	1.9 (1.0–3.8)	0.044
Ki-67 ≥20%	2.8 (1.4–5.4)	0.003	1.7 (0.8–3.4)	0.049
LVI positive	3.8 (2.0–7.2)	<0.001	2.2 (1.1–4.4)	0.031
Premenopausal status	1.6 (0.9–2.8)	0.12	1.3 (0.7–2.4)	0.43

Table 3. Stage and Nodal Distribution Across Molecular Subtypes (n=180)

Stage / Nodal Category	Luminal A (n=58)	Luminal B (n=47)	HER2-enriched (n=32)	TNBC (n=43)	Overall (n=180)
Stage I, n (%)	14 (24.1%)	4 (8.5%)	3 (9.4%)	5 (11.6%)	26 (14.4%)
Stage II, n (%)	26 (44.8%)	15 (31.9%)	7 (21.9%)	15 (34.9%)	63 (35.0%)
Stage III, n (%)	14 (24.1%)	22 (46.8%)	16 (50.0%)	17 (39.5%)	69 (38.3%)
Stage IV, n (%)	4 (6.9%)	6 (12.8%)	6 (18.8%)	6 (14.0%)	22 (12.2%)
N0, n (%)	32 (55.2%)	17 (36.2%)	8 (25.0%)	18 (41.9%)	75 (41.7%)
N1 (1–3 nodes), n (%)	14 (24.1%)	14 (29.8%)	10 (31.3%)	16 (37.2%)	54 (30.0%)
N2+ (≥4 nodes), n (%)	12 (20.7%)	16 (34.0%)	14 (43.8%)	9 (20.9%)	51 (28.3%)

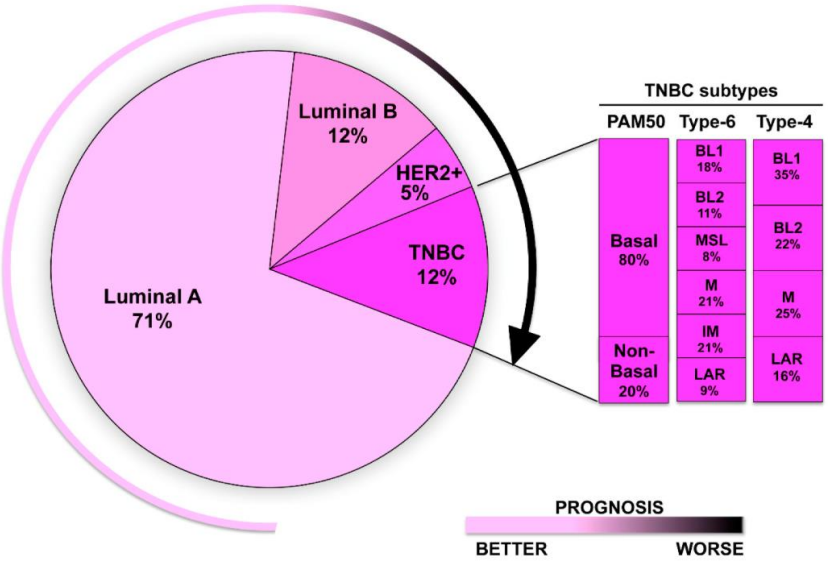

Figure 1. Grouped bar charts showing (A) molecular subtype distribution and (B) stage at diagnosis within each subtype in 180 breast carcinoma patients. TNBC (23.9%) and HER2-enriched (17.8%) subtypes show the highest proportion of Stage III–IV disease (74.4% and 68.8%, respectively), reflecting aggressive biological behaviour and late clinical presentation.

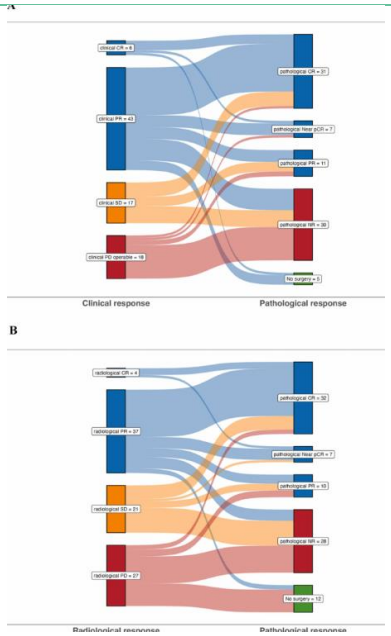

Figure 2. Sankey diagram illustrating patient flow from molecular subtype (left) through nodal category (middle) to stage group (right) in 180 breast carcinoma patients. HER2-enriched and TNBC subtypes demonstrate proportionally higher flows toward N2+ nodal category and Stage III–IV disease compared to Luminal A, visualising the clinical aggressiveness of high-risk breast cancer subtypes at diagnosis.

Discussion

This cross-sectional study of 180 breast carcinoma patients at a tertiary care hospital reveals a clinicopathological profile characterised by late-stage presentation (Stage III/IV at diagnosis in 50.6%), high TNBC prevalence (23.9%), and majority node-positive disease (58.3%) — all features that distinguish Indian breast cancer from that in high-income country cohorts and directly impact treatment intensity, prognosis, and survival. The ICMR National Cancer Registry Programme (NCRP) data consistently document 50–65% Stage III/IV at diagnosis in Indian tertiary cancer centres, compared to 20–25% in the United States where population mammographic screening has shifted the stage distribution leftward [7].

TNBC at 23.9% in our cohort is higher than the global average (15–20% of all breast cancers) and consistent with published Indian series reporting TNBC prevalence of 20–30%, particularly in premenopausal women [8,9]. The biological basis for the elevated TNBC prevalence in South Asian women remains incompletely understood — BRCA1/2 germline mutations, ethnicity-specific somatic mutation patterns, and environmental factors (dietary, reproductive) have all been proposed. The clinical implication is immediate: TNBC in the absence of targetable hormone receptors or HER2 relies on cytotoxic chemotherapy (anthracycline-taxane-based regimens) as the systemic backbone, with pembrolizumab (anti-PD-1) now approved for PD-L1-positive metastatic TNBC [10]. Access to these regimens, BRCA testing, and newer PARP inhibitors remains limited in the Indian public healthcare system, amplifying the importance of prevention-oriented interventions.

Tumour size >2 cm (aOR 3.1) as the strongest nodal predictor reflects the time-dependent accumulation of lymphatic metastases with tumour growth — a consequence of late presentation. Each 1 cm increase in tumour diameter is associated with approximately 15% increase in nodal positivity probability in published meta-analyses [6]. Lymphovascular invasion (LVI positive, aOR 2.2 in our analysis) is the microstructural

correlate of this process and is increasingly recognised as a sentinel feature justifying axillary dissection over sentinel node biopsy alone in clinical practice. HER2-enriched subtype showed the highest nodal positivity rate (75.0%), consistent with the known propensity of HER2-amplified tumours for early lymphatic dissemination through VEGF-C/D-mediated lymphangiogenesis [11].

Limitations: cross-sectional design captures a single time-point (diagnosis); FISH confirmation was performed for HER2 2+ equivocal cases but not routinely for 3+; genomic profiling (Oncotype DX, PAM50/Prosigna) was not available for routine Luminal A/B discrimination; 18-month enrolment window may not reflect seasonal or referral pattern variation; molecular subtype assignment used IHC surrogate criteria (St Gallen 2023) rather than mRNA profiling, with known classification discordance of 5–15%.

Conclusion

This Indian tertiary centre sees breast carcinoma mostly present in Stage III (38.3%) and with node positivity (58.3%) with TNBC being almost a quarter of the cases. Ki-67 ≥20%, LVI and tumour size and grade III histology, are all independent nodal positivity markers. The high burden at late stage places a strong emphasis on the importance of population-level screening programmes (clinical breast examination and mammography for women ≥40 years), awareness of self-breast examination and the availability of BRCA testing for high-risk young women with TNBC and/or family history.

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