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Original Research Article

Histopathological and Immunohistochemical Evaluation of Triple-Negative Breast Carcinoma: A Retrospective Study from a Tertiary Cancer Center

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Abstract:

Background: Triple-negative breast carcinoma (TNBC) is an aggressive breast cancer subtype characterized by lack of ER, PR, and HER2 expression. It is associated with poor prognosis and distinct pathological features.

Methods: A retrospective review of 120 breast carcinoma cases diagnosed in 2024 at a tertiary cancer center was performed. TNBC cases were identified by immunohistochemistry and compared with non-TNBC cases for histological grade, lymphovascular invasion, and basal marker expression.

Results: TNBC accounted for 40 cases (33.3%), with patients presenting at a younger mean age (47.2 years) compared to non-TNBC (54.6 years). High-grade tumors (Grade III) were more frequent in TNBC (80% vs. 40%). CK5/6 and EGFR positivity were observed in 70% and 65% of TNBCs, respectively.

Conclusion: TNBC constituted a third of all breast carcinomas and showed higher grade, younger age at presentation, and frequent basal marker positivity, underscoring its aggressive nature and prognostic significance.

Keywords: Triple-Negative Breast Carcinoma, Immunohistochemistry, CK5/6, EGFR, Basal-like breast cancer.

Introduction

Breast carcinoma is the most frequently diagnosed malignancy in women across the globe and represents a heterogeneous group of diseases with diverse morphological, molecular, and clinical characteristics. In India, breast cancer has overtaken cervical cancer as the leading cancer among women, with increasing incidence particularly in urban and peri-urban populations [1].

In the molecular subtypes of breast carcinoma, TNBC represent about 15–20% of cases and is defined by the absence of progesterone receptor, human epidermal growth factor receptor 2 (HER2), estrogen receptor, and expression on immunohistochemistry [2,3]. TNBC typically affects younger women and is linked to aggressive clinical behavior, high-grade histology, early recurrence, and poor prognosis. Due to the lack of actionable hormone or HER2 targets, systemic chemotherapy remains the mainstay of treatment [4].

From a pathological standpoint, TNBCs often present as invasive ductal carcinomas of no special type (IDC-NST) and are more likely to demonstrate features such as geographic necrosis, pushing margins, central fibrosis, and high mitotic index [5]. Immunohistochemically, a significant proportion of TNBCs express basal cytokeratins (CK5/6) and EGFR, aligning them with the basal-like subtype described in genomic studies [6,7]. These markers may offer potential avenues for targeted therapies in the future.

Given the clinical importance and unique biology of TNBC, evaluating its histopathological and immunohistochemical profile remains critical for understanding disease behavior and guiding prognostication. Despite its high prevalence and aggressive course, limited data exists from eastern India, particularly from specialized oncology centers.

This study aimed to evaluate the histomorphological features and IHC profiles of TNBC cases diagnosed at the Acharya Harihar Postgraduate Institute of Cancer (AHPGIC), Cuttack, during a one-year period. The findings are compared with non-TNBC cases to identify significant pathological and immunophenotypic differences, with emphasis on proliferative index (Ki-67) and basal marker expression (CK5/6, EGFR).

Methods

Study Design and Setting: This retrospective study carried out the Department of Pathology at AHPGIC, located in eastern India, Cuttack serves as a tertiary cancer referral center. This study was

carried out over a one-year period, spanning from January to December 2024.

Study Population: A total of 120 histologically confirmed cases of invasive breast carcinoma confirmed through histological examination. Clinical and pathological information was gathered from hospital records and histopathology requisition forms.

Inclusion Criteria

- Female individuals diagnosed with invasive breast carcinoma.
- Cases with complete immunohistochemical profiling including ER, PR, and HER2.
- Adequately preserved tissue blocks available for further IHC staining (CK5/6, EGFR, Ki-67).

Exclusion Criteria

- Recurrent breast carcinoma or metastatic lesions.
- Inadequate tissue samples or missing IHC data.
- Cases with ambiguous HER2 IHC results without confirmatory FISH testing.

Histopathological Evaluation: All H&E stained slides were independently examined by two pathologists. Tumors were classified based on the WHO 2019 classification of breast tumors. Grading was done using the Nottingham histologic grading system.

Histomorphological parameters analyzed included:

- Tumor subtype (IDC-NST, metaplastic, others)
- Tumor grade
- Lymphovascular invasion
- Tumor necrosis
- Stromal response

Immunohistochemistry (IHC): IHC was carried out on paraffin-embedded (FFPE), formalin-fixed, tissue sections using the streptavidin–biotin-peroxidase technique on an automated immunostainer.

Interpretation Criteria:

- ER/PR: Positive if ≥1% nuclear staining in tumor cells (ASCO/CAP guidelines) [1].
- HER2: Scored 0 to 3+; 3+ considered positive. 2+ considered equivocal and excluded unless FISH was available.
- Ki-67: Expressed as percentage of positively stained tumor cell nuclei. A cutoff of >20% was considered high proliferation.
- CK5/6 & EGFR: Considered positive if ≥10% of tumor cells showed membranous and/or cytoplasmic staining.

Based on IHC results:

- TNBC: Tumors negative for ER, PR, and HER2.
- Non-TNBC: Tumors positive for at least one of the three markers.

Statistical Analysis: Data were compiled in Microsoft Excel and analyzed using SPSS version 25.0 (IBM Corp.). Clinicopathological variables were summarized using descriptive statistics. For comparison between TNBC and non-TNBC groups, while continuous variables were assessed using the Student's t-test, categorical variables were analyzed using the Chi-square test or Fisher's exact test. Statistically significant as p-value below 0.05.

Ethical Considerations: Institutional Ethics Committee approval was obtained prior to initiation of the study (Approval No. AHPGIC/IEC/2024/027). Since this was a retrospective analysis of anonymized data, informed consent was waived.

Results

Total 120 histologically confirmed cases of invasive breast carcinoma were included in the study. Based on immunohistochemical profiling, 40 cases (33.3%) were identified as TNBC, while the remaining 80 cases (66.7%) were categorized as non-TNBC. The mean ± SD age of patients with TNBC was 47.2 ± 8.4 years, and for the non-TNBC group, a mean ± SD age of 54.6 ± 9.1 years. A majority of the TNBC cases (67.5%) were seen in patients below 50 years of age, whereas only 35% of non-TNBC cases fell into this age group.

Histologically, Grade III tumors were importantly more frequent in the TNBC group, seen in 80% of cases, compared to 41% in the non-TNBC group. Tumor necrosis was observed in 65% of TNBC cases and 35% of non-TNBC cases, while LVI was identified in 60% of TNBCs compared to 36% of non-TNBCs. In terms of histologic subtype, IDC-NST was the predominant pattern in both groups, accounting for 90% of TNBC and 85% of non-TNBC cases. Metaplastic carcinoma was noted in 7.5% of TNBC cases and 1.25% of non-TNBC cases.

Immunohistochemical analysis revealed that high Ki-67 expression (>20%) was more common in the TNBC group, observed in 85% of cases compared to 50% in the non-TNBC group. Basal cytokeratin marker CK5/6 showed positivity in 70% of TNBC cases, while only 15% of non-TNBCs expressed this marker. Similarly, EGFR expression was noted in 65% of TNBC cases versus 20% of non-TNBC cases, indicating a strong association of these markers with the TNBC phenotype.

Further analysis showed that among the TNBC group, 31 cases (77.5%) exhibited a basal-like phenotype, defined by the presence of CK5/6 and/or

EGFR expression. These basal-like TNBCs tended to show higher histologic grade, more frequent necrosis, and elevated Ki-67 proliferation indices compared to non-basal TNBCs, although statistical comparisons within TNBC subgroups were not performed due to small sample size.

Table 1: Comparison of Clinicopathological and Immunohistochemical Features Between TNBC and Non-TNBC Cases (n = 120)

Parameter	TNBC (n = 40)	Non- TNBC (n = 80)	p-value
Mean ± SD (Age years)	47.2 ± 8.4	54.6 ± 9.1	0.01
Age <50 years	27 (67.5%)	28 (35%)	0.002
Grade III tumors	32 (80%)	32 (40%)	<0.001
Tumor necrosis present	26 (65%)	28 (35%)	0.002
Lymphovascular invasion	24 (60%)	29 (36%)	0.01
IDC NST subtype	36 (90%)	68 (85%)	0.47
Metaplastic carcinoma	3 (7.5%)	1 (1.25%)	0.08
Ki-67 > 20%	34 (85%)	40 (50%)	0.001
CK5/6 positivity	28 (70%)	12 (15%)	<0.001
EGFR positivity	26 (65%)	16 (20%)	<0.001
Basal-like phenotype	31 (77.5%)	0	-

Discussion

Triple-negative breast carcinoma (TNBC) is recognized worldwide as an aggressive subtype, but its prevalence varies across populations. In our study, TNBC constituted 33.3% of all invasive breast carcinoma cases, which is considerably higher than the 15–20% typically reported in Western cohorts (1,2). This elevated prevalence aligns with Indian studies reporting TNBC rates ranging from 25% to 35% (3,4), suggesting possible geographic, genetic, and lifestyle differences that warrant further investigation. Importantly, the younger mean age of presentation in our TNBC group (47.2 years) compared to non-TNBC patients mirrors the trend described in prior Indian studies, where TNBC more often affects premenopausal women (5).

Histopathologically, TNBCs in our series demonstrated aggressive features, including a predominance of high-grade tumors, frequent necrosis, and increased lymphovascular invasion. While such characteristics are well-documented globally (6), the higher frequency observed in Indian cohorts may contribute to poorer outcomes, particularly in resource-limited settings where access to advanced therapies is restricted.

From an immunohistochemical perspective, the high Ki-67 proliferation index observed in TNBC cases reinforces the aggressive biology of this subtype, consistent with reports from Dent et al. and Bianchini et al. (6,7). A key finding of our study was the high proportion (77.5%) of TNBCs exhibiting a basal-like phenotype, characterized by CK5/6 and/or EGFR expression. This aligns with studies by Nielsen et al. and Rakha et al. (8,9), which highlight basal-like TNBCs as a clinically relevant subgroup. Although current treatment remains largely confined to chemotherapy, basal-like TNBCs are being actively investigated for targeted therapies, including EGFR inhibitors, PARP inhibitors, and immune checkpoint inhibitors (10,11). Identifying these markers in routine practice can thus help stratify patients for emerging treatment opportunities.

The retrospective design of this study introduces inherent biases, including reliance on archived data and absence of follow-up. Survival outcomes could not be assessed, limiting prognostic evaluation. Furthermore, HER2 2+ cases without confirmatory FISH testing were excluded, potentially underestimating equivocal HER2 expression. Future studies with larger cohorts, prospective design, and inclusion of molecular profiling are needed to validate these findings and assess survival implications.

Conclusion

This retrospective study highlights the distinct clinicopathological and immunohistochemical characteristics of TNBC in patients from a tertiary cancer center in Eastern India. TNBCs occurred predominantly in younger women and exhibited aggressive histological features, including higher grade, greater necrosis, and increased lymphovascular invasion.

A particularly important finding was the high prevalence of basal-like TNBCs, with frequent CK5/6 and EGFR positivity. These markers are simple, cost-effective, and widely available, making them practical tools for risk stratification in low-resource settings where advanced molecular testing is not feasible. Their routine use in diagnostic practice can help identify high-risk patients and guide selection for clinical trials exploring targeted therapies such as EGFR inhibitors, PARP inhibitors, and immunotherapy.

Given the retrospective design and lack of survival data, further prospective, multi-center studies with

long-term follow-up are essential to validate these findings, establish prognostic value, and explore therapeutic implications of basal marker expression in TNBC.

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