Original Article

Immunohistochemical Profile and Molecular Subtype Distribution of Breast Carcinoma at a Tertiary Care Centre in Western Rajasthan

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ABSTRACT

Introduction: Breast cancer is a heterogeneous disease, and immunohistochemistry-based molecular subtyping serves as a marker for intrinsic classification. The distribution of molecular subtypes shows considerable regional variation across India, with important implications for prognosis and treatment planning.

Aim: To evaluate the immunohistochemical profile and molecular subtype distribution of breast carcinoma cases at a tertiary care centre in western rajasthan.

Materials and Methods: This retrospective observational study included **239 cases** of histopathologically confirmed invasive breast carcinoma. Estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) status were assessed using standard immunohistochemistry protocols. Molecular subtypes were classified into luminal A, luminal B, HER2-enriched, and triple-negative breast cancer (TNBC) based on surrogate immunohistochemical markers. Data were analysed descriptively.

Results: ER positivity was observed in 226 cases (94.6%), and PR positivity in 228 cases (95.4%). HER2 overexpression (3+) was identified in 82 cases (34.3%). Luminal A was the most common molecular subtype (153 cases, 64.0%), followed by luminal B (78 cases, 32.6%). HER2-enriched and triple-negative subtypes were infrequent, accounting for 4 cases each (1.7%).

Conclusion: The present study demonstrates a marked predominance of luminal breast cancer subtypes with a comparatively low frequency of TNBC. While luminal dominance is consistent with several Indian studies, the low TNBC prevalence highlights significant regional and methodological variation. Specific molecular profiling remains essential for understanding local disease pathology and optimizing personalized breast cancer management.

Keywords: Breast cancer; Immunohistochemistry; Molecular subtypes; Luminal breast cancer; Triple-negative breast cancer.

INTRODUCTION

Breast cancer is the most common malignancy among women worldwide and represents a major public health problem, with a steadily increasing incidence in low- and middle-income countries including India[1]. In India, breast cancer has surpassed cervical cancer as the leading cancer among urban women, with a significant proportion of patients presenting at a younger age and with advanced disease compared to western populations[2].

Breast cancer is a heterogeneous disease, and traditional clinicopathological parameters alone are insufficient to predict prognosis and therapeutic response[3]. Advances in molecular biology have led to the identification of distinct molecular

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subtypes—luminal A, luminal B, HER2-enriched, and triple-negative breast cancer—each associated with different biological behaviour and therapeutic implications[1].

Due to the high cost and limited availability of gene expression profiling, immunohistochemistry-based surrogate classification using estrogen receptor, progesterone receptor, HER2, and Ki-67 has become the standard method for molecular subtyping in routine practice, particularly in resource-limited settings[4]. This approach is endorsed by international consensus guidelines and shows good correlation with intrinsic molecular subtypes[5].

Several studies have demonstrated a molecular subtype distribution distinct from western literature, with a higher prevalence of hormone receptor–positive tumours and wide inter-regional variation[6]. Indian studies have also reported a relatively higher burden of triple-negative breast cancer compared to western populations, although the reported prevalence varies considerably across institutions[7].

In view of these variations, institution-specific data remain essential to understand regional disease biology and guide optimal treatment strategies. The present study therefore evaluates the immunohistochemical profile and molecular subtype distribution of breast carcinoma cases in western rajasthan and compares the findings with existing Indian literature[8].

MATERIALS AND METHODS

This was a retrospective, observational study conducted in the Department of Pathology at Dr. S. N. Medical College, Jodhpur, over a five-year period from 2021 to 2025.. All consecutive cases of histopathologically confirmed invasive carcinoma of the breast for which immunohistochemical evaluation of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) was performed were included in the study. Both core biopsy specimens and modified radical mastectomy (MRM) specimens were considered Cases with incomplete immunohistochemical data or inadequate tissue for interpretation were excluded from molecular subtype analysis.

Variables recorded included patient age, biopsy number, histopathological diagnosis, Bloom–Richardson score, presence of lymphovascular invasion/perineural invasion, ER status, PR status, HER2 score, lymph node status, neoadjuvant chemotherapy history, skin involvement, and TNM staging where available. All specimens were fixed in 10% neutral buffered formalin and processed routinely. Haematoxylin and eosin–stained sections were reviewed to confirm the diagnosis and histological subtype. Tumour grading was performed using the modified Bloom–Richardson grading system wherever applicable. Lymphovascular and perineural invasion were assessed on available sections.

Immunohistochemical staining for ER, PR, and HER2 was performed on representative tumour sections using standard laboratory protocols.
- **ER and PR** expression was assessed based on nuclear staining and reported using the Allred scoring system. Tumours showing ≥2% nuclear positivity were considered receptor positive.
- **HER2** status was evaluated based on membrane staining intensity and pattern and scored as 0, 1+, 2+, or 3+ according to ASCO/CAP guidelines.
  Cases with HER2 score 0 or 1+ were considered negative, while cases with a score of 3+ were considered positive. HER2 equivocal (2+) cases were not included in definitive molecular subtype categorization if confirmatory testing was not available.

Based on immunohistochemical surrogate markers, breast carcinomas were classified into the following molecular subtypes:
- **Luminal A**: ER and/or PR positive and HER2 negative
- **Luminal B**: ER and/or PR positive and HER2 positive
- **HER2-enriched**: ER negative, PR negative, HER2 positive
- **Triple-negative breast cancer (TNBC)**: ER negative, PR negative, HER2 negative

Data were entered into Microsoft Excel and analysed descriptively. Categorical variables were expressed as frequencies and percentages. Results were summarized using tables and graphical representations.

RESULTS

A total of 239 cases of breast carcinoma with complete immunohistochemical data were included in the study. All cases were female patients, and all tumors were histopathologically confirmed invasive breast carcinomas. The age of patients ranged from 26 to 90 years, with a mean age of 53.1 ± 13.3 years and a median age of 53 years. The distribution of cases by age groups showed that 9 patients (3.8%) were aged ≤30 years, 36 (15.1%) were between 31–40 years, 57 (23.8%) between 41–50 years, 56 (23.4%) between 51–60 years, 47 (19.7%) between 61–70 years, 18 (7.5%) between 71–80 years, and 6 patients (2.5%) were older than 80 years. (Figure 1)

Diagnosis was established on core biopsy specimens in 146 cases (61.1%) and modified radical mastectomy (MRM) specimens in 93 cases (38.9%). Invasive ductal carcinoma constituted the predominant histological subtype. An associated ductal carcinoma in situ (DCIS) component was identified in 40 cases (16.7%). Tumour grading using the modified Bloom–Richardson grading system was present in 109 cases (45.6%).

Immunohistochemical evaluation demonstrated estrogen receptor (ER) and/or progesterone receptor (PR) positivity in 222 cases (92.9%), HER2 overexpression (IHC 3+) was observed in 4 cases (1.7%).(Figure 2) Based on immunohistochemical surrogate classification, tumors were categorized into molecular subtypes, with the luminal subtype accounting for 222 cases (92.9%), triple-negative breast cancer (ER−/PR−/HER2−) identified in 13 cases (5.4%), and HER2-enriched subtype (ER−/PR−/HER2 3+) seen in 4 cases (1.7%).(Figure 3-5)

Assessment of lymphovascular and/or perineural invasion (LVI/PNI) revealed positivity in 45 cases (18.8%). Lymph node status was positive for metastasis in 59 cases (24.7%).
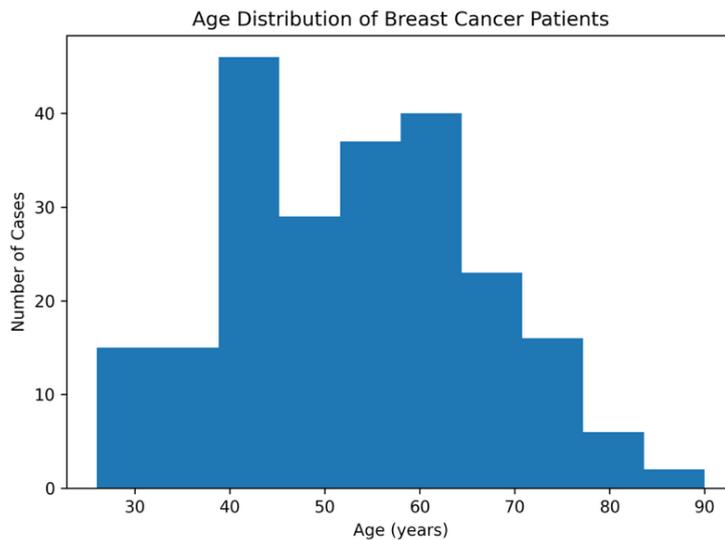

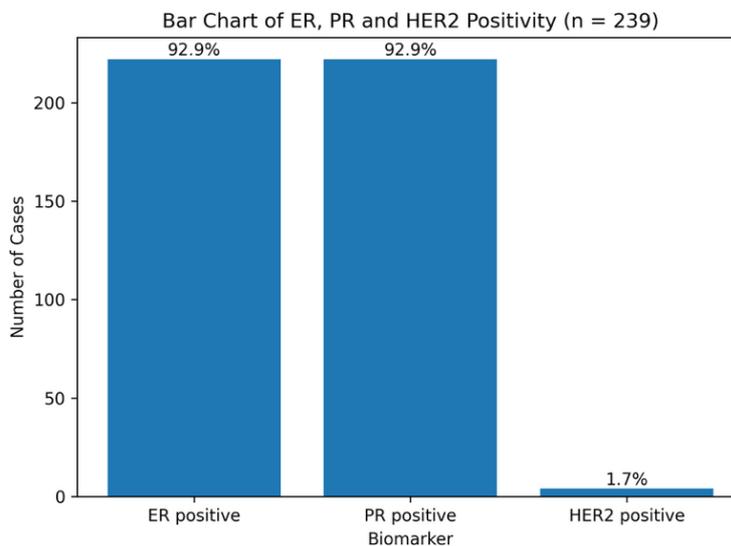**Figure 1:- Age distribution of breast cancer patients**

Figure 2:- Comparative bar chart of ER, PR, and HER2/neu expression in breast cancer patients
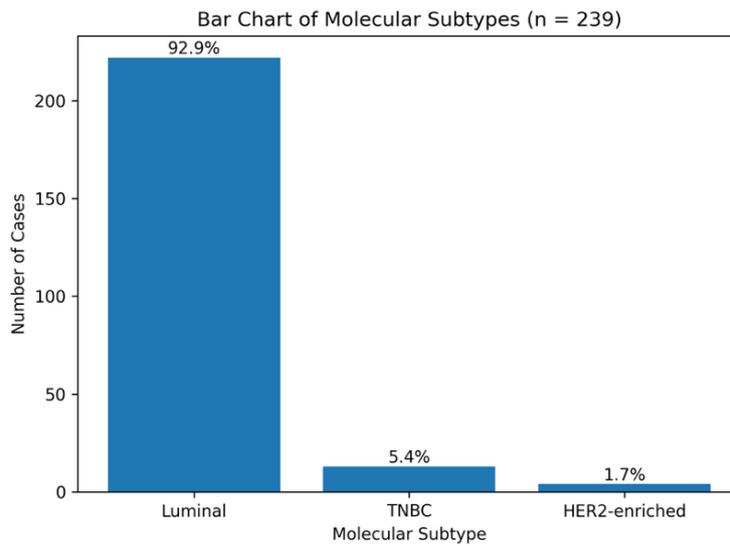
Bar Chart of Molecular Subtypes (n = 239)

Figure 3 :- Bar chart showing estrogen receptor (ER), progesterone receptor (PR), and HER2/neu positivity among breast carcinoma cases (n = 239).
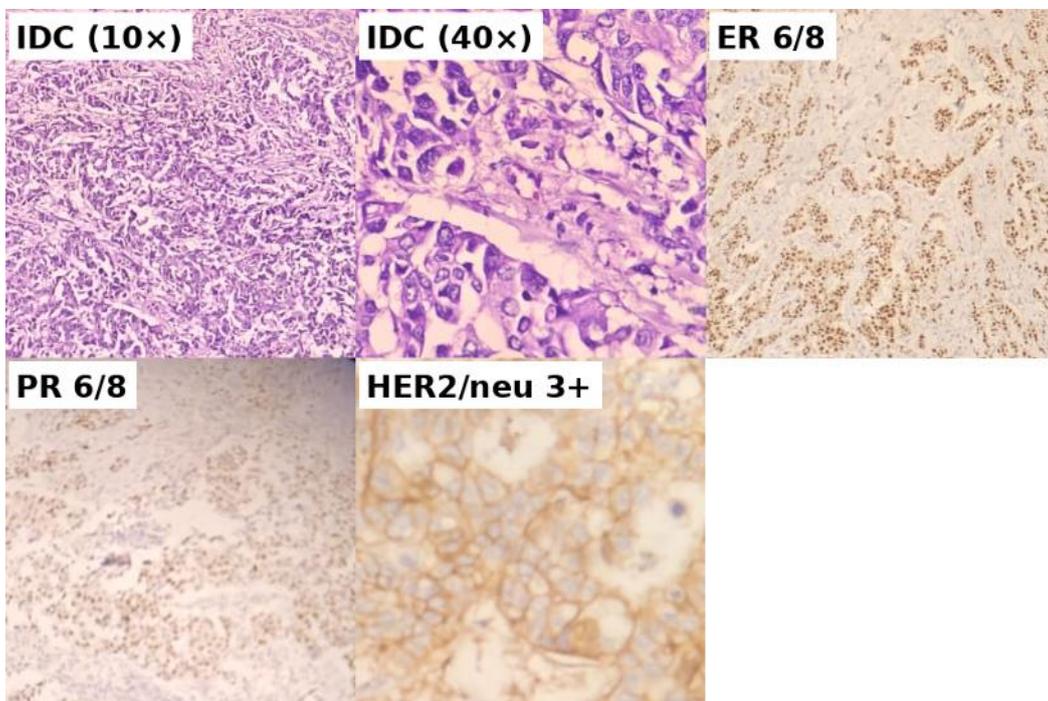

Figure 4 :- Histopathological and immunohistochemical features of invasive ductal carcinoma showing IDC morphology (10×, 40×), ER and PR expression and HER2/neu status
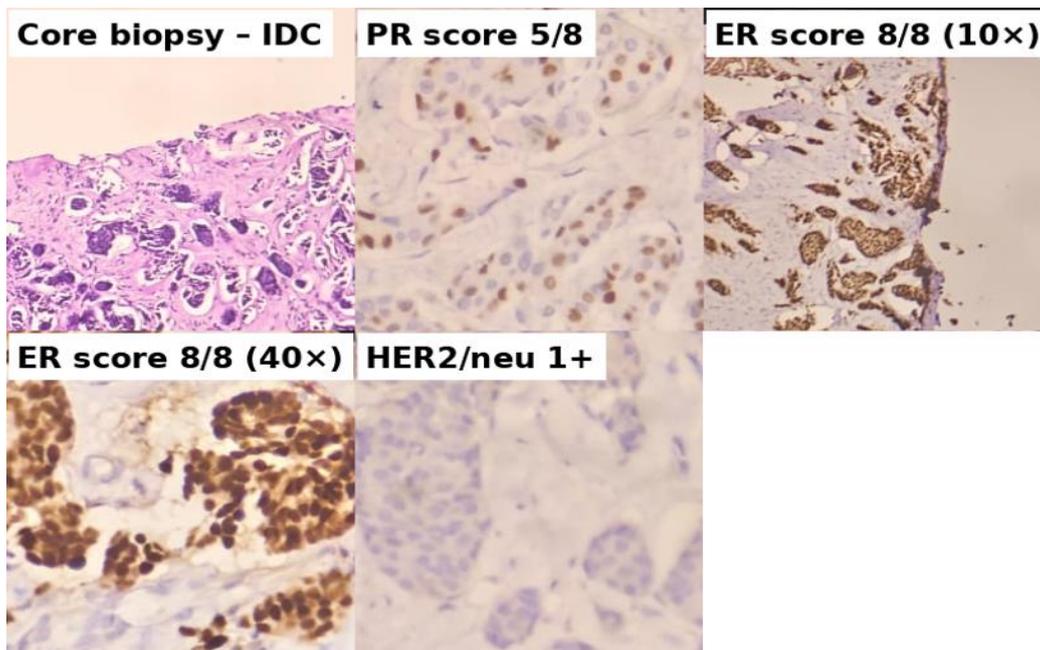
Figure 5 :- Histopathological and immunohistochemical features of invasive ductal carcinoma showing IDC morphology (10×, 40×), ER and PR expression and HER2/neu status

DISCUSSION

Breast cancer is a heterogeneous disease, and molecular subtyping using immunohistochemical surrogate markers has become integral to prognostication and therapeutic decision-making in routine clinical practice[1]. In the present study, luminal subtypes constituted the majority of cases, with luminal A being the most prevalent, followed by luminal B, while HER2-enriched and triple-negative breast cancers were relatively infrequent. The predominance of luminal breast cancer is also observed in other study[2]. Studies from western and northern India have similarly demonstrated a higher proportion of hormone receptor–positive tumours, often accounting for more than half of all breast cancer cases[3]. These findings contrast with earlier assumptions that breast cancer pathology is predominantly characterized by aggressive subtypes.

However, the proportion of triple-negative breast cancer (TNBC) in the present cohort is considerably lower than that reported in many Indian studies, where TNBC prevalence has commonly ranged between 20% and 35%[4]. Large systematic reviews and meta-analyses from India have consistently demonstrated a higher pooled prevalence of TNBC compared to western populations[5], making the low TNBC frequency observed in the current study noteworthy.

The high prevalence of luminal tumours in this study may be explained by multiple factors. First, the cohort demonstrated very high estrogen and progesterone receptor positivity, which directly translates into a higher luminal subtype burden. Referral patterns to a tertiary care center, with a predominance of operable or biopsy-diagnosed cases, may preferentially capture hormone receptor–positive disease.

Second, regional variation within India is well recognized. Differences in demographic characteristics, reproductive factors, lifestyle changes, and genetic background may influence molecular subtype distribution across different parts of the country[6]. Increasing awareness, earlier diagnosis, and improved access to healthcare services may further contribute to a higher detection rate of luminal tumors, which generally exhibit a more indolent clinical course.

The relatively low frequency of TNBC observed in this study may partly be attributed to methodological factors. Molecular subtyping was performed using immunohistochemical surrogate markers without incorporation of the Ki-67 proliferation index. In the absence of Ki-67, some tumors that may be classified as luminal B in other studies could have been categorized as luminal A, thereby increasing the apparent luminal subtype proportion[7].

Additionally, HER2-equivocal (2+) cases without confirmatory in-situ hybridization were excluded from definitive subtype classification, which may have influenced the final subtype distribution. The single-center nature of the study and institutional laboratory practices may further contribute to variation when compared with multicentric or population-based studies[5].

Despite these differences, the findings of the present study highlight the importance of institution-specific molecular profiling. The predominance of luminal subtypes emphasizes the central role of endocrine therapy in breast cancer

management in this setting, while the relatively low burden of TNBC suggests a smaller subset of patients requiring aggressive chemotherapy-based treatment strategies[8].

Limitations

The retrospective study design, single-institution setting, lack of Ki-67 data, and absence of confirmatory testing for HER2-equivocal cases are important limitations and should be considered while interpreting the results.

CONCLUSION

In conclusion, this study demonstrates a predominance of luminal breast cancer subtypes with a comparatively low frequency of TNBC in this institutional cohort. Although luminal dominance is consistent with Indian literature, the low TNBC prevalence highlights significant regional and methodological variation. These findings reinforce the need for region- and institution-specific molecular data to better understand breast cancer biology in India and to guide personalized treatment approaches[8].

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