

Immunohistochemical Pattern of Breast Cancer Patients from a Limited Geographical Region of Tamil Nadu, India: A Retrospective Study

RAJIV KUMAR KRISHNAN¹, R VISHNUSRI²


ABSTRACT

Introduction: Breast Cancer is the leading cause of cancer incidence worldwide among females, accounting for 11.6% of all cancers, with an estimated mortality rate of 6.9%, ranking fourth according to Global Cancer Observatory (GLOBOCAN) 2022 statistics. Over the years, BC treatment evolved from being based solely on clinical findings to pathological findings and is now primarily guided by the molecular characteristics of individual tumour types. Current American Joint Committee on Cancer (AJCC) staging and National Comprehensive Cancer Network (NCCN) recommendations are largely based on molecular features of the disease.

Aim: To analyse the pattern of molecular immunohistochemical expression in a limited geographical area of the study centre, with specific reference to luminal subtypes of BC.

Materials and Methods: This retrospective study was conducted at the Department of Radiation Oncology, Government Villupuram Medical College and Hospital (GVMCH), Villupuram, Tamil Nadu, India. Immunohistochemistry (IHC) data from 343 BC patients were analysed. Data were collected from female patients with histologically confirmed BC

who had available IHC results between 2014 and 2024. Oestrogen Receptor (ER), Progesterone Receptor (PR), HER2/neu expression, and the proliferation index (Ki-67) were recorded. Cases were grouped according to luminal subtype classification. Associations between individual receptor expression, luminal subtypes, and proliferation index were evaluated. Descriptive statistics were used to summarise demographic and biomarker characteristics. Associations between categorical variables were assessed using the chi-square test. A p-value < 0.05 was considered statistically significant.

Results: Of the 343 patients analysed, 137 (39.9%) were classified as Luminal A, 54 (15.7%) as Luminal B, 52 (15.2%) as Human Epidermal Growth Factor Receptor 2 (HER2/neu)-enriched, and 100 (29.2%) as basal-like subtype. Among the 191 patients with available Ki-67 data, 141 (73.8%) demonstrated a proliferation index greater than 20%.

Conclusion: The present study demonstrated that Luminal A was the most prevalent subtype, followed by the basal-like, Luminal B, and HER2/neu-enriched subtypes in this geographical population. This distribution differs slightly from patterns reported in other published studies.

Keywords: Breast neoplasm, Biomarkers, Oestrogen receptor, Progesterone receptor

INTRODUCTION

Breast Cancer (BC) is the second most common cancer worldwide and the fourth leading cause of cancer-related mortality, according to Global Cancer Observatory (GLOBOCAN) 2022 statistics [1]. Hippocrates described BC as a systemic disease as early as 460-377 Before Christ (B.C.) [2], however, local treatment strategies such as Halsted's radical mastectomy later demonstrated favourable outcomes in terms of local recurrence and survival [3]. The introduction of systemic chemotherapy significantly transformed BC management [4], reinforcing the earlier systemic concept proposed by Hippocrates.

In the modern era of molecular pathology, targeted therapy has assumed a pivotal role in BC management. Classification of BC into molecular subtypes facilitates risk stratification, treatment personalisation, and improved clinical outcomes [5].

The standard molecular panel used in BC evaluation includes Oestrogen Receptor (ER), Progesterone Receptor (PR), Human Epidermal Growth Factor Receptor 2 (HER2/neu), and the proliferation marker Ki-67. The relevance of hormonal receptors originated from observations that breast tumors regressed following oophorectomy, as demonstrated by Beatson in 1896 [6]. This concept led to the identification of the oestrogen receptor in 1961 [7]. These biomarkers have been shown to variability based on age, ethnicity, race, and cultural factors.

Most published data originate from Western populations or heterogeneous cohorts from South Asia, which do not adequately

reflect regional variations within India or across individual states. Therefore, the present study aimed to evaluate the molecular immunohistochemical pattern of BC with respect to luminal subtypes in a limited geographical area.

MATERIALS AND METHODS

This retrospective study was conducted at the Department of Radiation Oncology, Government Villupuram Medical College and Hospital (GVMCH), Villupuram, Tamil Nadu, India. The study involved a review and analysis of medical records and pathology reports of BC patients registered at the Institution. Approval was obtained from the Institutional Scientific Research Committee and Institutional Ethics Committee prior to study initiation (IEC Approval No: GVMC/IEC/2021/04).

Data from BC patients diagnosed between 2014 and 2024 were collected according to predefined inclusion and exclusion criteria. Data collection and analysis were performed between March 2025 and September 2025.

Inclusion criteria:

- Female patients with histologically confirmed BC;
- Availability of ER, PR, and HER2/neu IHC results;
- Patients with or without documented Ki-67 proliferation index were included to ensure comprehensive cohort representation and.
- Cases reported between 2014 and 2024 were included in the study.

Exclusion criteria:

- Male BC patients;
- Incomplete or missing ER/PR/HER2/neu data and
- Duplicate or unreadable records were excluded.

Study Procedure

Data were extracted from records maintained in the Department of Radiation Oncology, Government Villupuram Medical College and Hospital. The following variables were recorded:

- Demographic details (age at diagnosis)
- Histopathological diagnosis
- ER, PR, and HER2/neu status
- Ki-67 proliferation index (%) where available

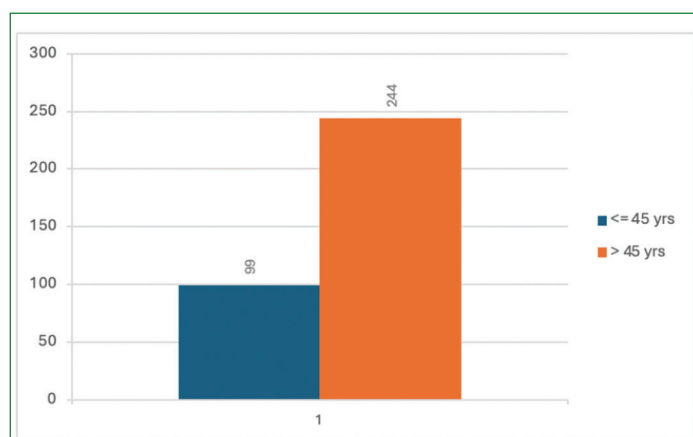
A total of 343 patient records were analysed, all of which included ER, PR, and HER2/neu status. Among these, Ki-67 data were available for 191 patients. Tumours were classified into luminal subtypes based on St. Gallen consensus recommendations [5]. The present study presents the luminal subtype distribution among BC patients from a limited geographical area, predominantly representing a low socioeconomic population.

STATISTICAL ANALYSIS

All extracted data were entered into a secure Microsoft Excel spreadsheet and cross-verified for accuracy. Statistical analysis was performed using IBM Statistical Package for the Social Sciences (SPSS) Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarise demographic and biomarker characteristics. Associations between categorical variables were assessed using the Chi-square test. Subgroup analyses were performed for cases with available Ki-67 data. A p-value<0.05 was considered statistically significant.

RESULTS

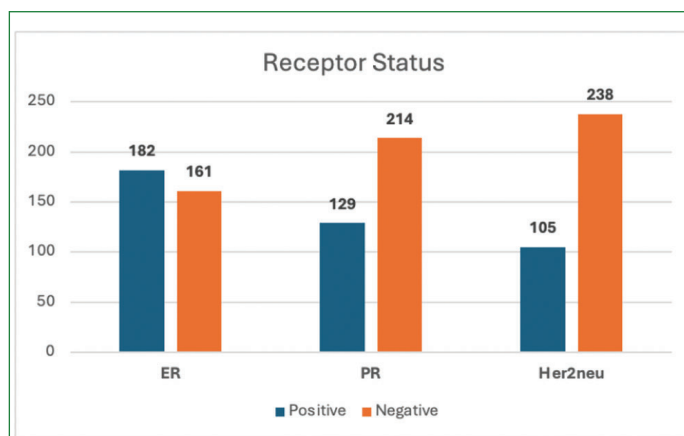
A total of 343 female BC patients were included in the study. Of these, 99 patients were younger than 45 years, while 244 patients were older than 45 years (28.9% vs. 71.1%) [Table/Fig-1]. Left-sided BC was observed in 164 patients, and right-sided disease in 179 patients (47.8% vs. 52.2%). The patients belonged to 32 different talukas/zillas across five districts of Northern Tamil Nadu.



[Table/Fig-1]: Age-wise distribution of cases

With respect to ER status, 182 patients were positive and 161 were negative (53.1% vs. 46.9%). For the PR, 129 patients were positive and 214 were negative (37.6% vs. 62.4%). Regarding HER2/neu expression, 105 patients were positive and 238 were negative (30.6% vs. 69.4%) [Table/Fig-2].

These data were subsequently classified into intrinsic molecular subtypes—Luminal A, Luminal B, HER2-enriched, and Basal-like—based on St. Gallen consensus recommendations. Among the 343 patients, Luminal A was the most prevalent subtype, comprising



[Table/Fig-2]: Distribution of receptor positivity pattern.

137 patients (39.9%). This was followed by the Basal-like subtype with 100 patients (29.2%), Luminal B subtype with 54 patients (15.7%), and HER2-enriched subtype with 52 patients (15.2%) [Table/Fig-3].

Intrinsic subtype	n (%)
Luminal A	137 (39.9)
Luminal B	54 (15.7)
HER2-enriched	52 (15.2)
Basal-like	100 (29.2)
Total	343 (100.0)

[Table/Fig-3]: Distribution of intrinsic molecular subtypes.

When age was compared with luminal subtype among all 343 patients, no statistically significant association was observed (p-value=0.983) [Table/Fig-4].

Parameters		Intrinsic Subtype				Total	p-value
		Luminal A	Luminal B	Her2-enriched	Basal-like		
Age	≤45 yrs	Count	38	16	15	30	0.983
		%	27.7%	29.6%	28.8%	30.0%	
	>45 yrs	Count	99	38	37	70	
		%	72.3%	70.4%	71.2%	70.0%	
Total	Count	137	54	52	100	343	
	%	100.0%	100.0%	100.0%	100.0%	100.0%	

Chi-square Tests

[Table/Fig-4]: Age and intrinsic subtype.

Among the 343 patients, Ki-67 proliferation index data were available for 191 patients. Of these, 50 patients had a Ki-67 index <20%, while 141 patients had a Ki-67 index >20% (26.2% vs. 73.8%). The association between proliferation index and luminal subtype was analysed in these 191 patients, and no statistically significant association was found (p-value=0.383) [Table/Fig-5].

Ki-67			Intrinsic subtype				Total	p-value
			Luminal A	Luminal B	Her2 enriched	Basal-like		
<20%	Count	25	5	4	16	50	0.383	
		%	30.5%	18.5%	16.0%	28.1%		
	≥20%	Count	57	22	21	41		141
		%	69.5%	81.5%	84.0%	71.9%		
Total	Count	82	27	25	57	191		
	%	100.0%	100.0%	100.0%	100.0%			

Chi-square test

[Table/Fig-5]: Proliferative Index (Ki-67) and intrinsic subtype.

DISCUSSION

BC has been one of the most extensively studied malignancies since the era of Hippocrates and is among the cancers with the highest five-year relative survival rates, ranging from 91% in developed countries such as the United States [8] to 66.4% in developing countries like India [9]. Improvements in survival have largely resulted from earlier detection through widespread screening programs and individualised treatment strategies based on molecular profiling.

Towards the end of the 20th century, the management of BC evolved significantly with the introduction of modern chemotherapeutic agents and advanced radiotherapy techniques, leading to improved survival outcomes. Advances in the understanding of molecular characteristics, including hormone receptor expression (ER and PR) and HER2/neu overexpression, have provided valuable prognostic information and enabled personalised treatment approaches [10].

Clinical presentation varies based on factors such as age, stage of disease, and molecular profile, all of which influence treatment planning. In the present study, 99 patients (28.9%) were younger than 45 years and 244 patients (71.1%) were older than 45 years, a distribution similar to that reported in Western populations [11]. However, previous Indian data suggest that approximately 48% of BC patients are younger than 50 years [12].

Regarding laterality, 164 patients (47.8%) had left-sided BC and 179 patients (52.2%) had right-sided disease. This contrasts with previously published data, which generally report left-sided predominance [13].

In the present study, ER positivity was observed in 53.1%, PR positivity in 37.6%, and HER2/neu positivity in 30.6% of patients. Compared with standard published data, the present study demonstrated lower ER and PR positivity, suggesting a higher proportion of hormone-resistant tumours [14]. HER2 positivity was at the upper end of the reported range [15], indicating a greater proportion of patients potentially eligible for HER2-targeted therapy. These differences are likely attributable to regional and ethnic variations, as South Asian populations have been shown to exhibit lower ER/PR expression and higher HER2/neu expression [16-18].

Among the 343 patients, Luminal A subtype was the most prevalent (39.9%), followed by Basal-like (29.2%), Luminal B (15.7%), and HER2-enriched subtypes (15.2%). When compared with the Surveillance, Epidemiology, and End Results Program (SEER) and other standard datasets, Luminal A and B subtypes were comparable, whereas HER2-enriched and Basal-like subtypes were relatively more common in the present study [Table/Fig-6] [19,20].

Intrinsic subtypes	Present study	SEER data (20)	Standard data (19)	Comparison
Luminal A	39.9%	70%	34.7-54%	Within expected range
Luminal B	15.7%	9%	12.7-17.3%	Matches with standard
HER2-enriched	15.2%	4%	5.6-24.1%	Slightly higher
Basal-like	29.2%	11%	21.5-31.6%	Much higher than average

[Table/Fig-6]: Comparison of the study data with standard published data [19,20].

Of the 191 patients with available Ki-67 data, 141 patients (73.8%) had a proliferation index >20%, suggesting aggressive tumour biology, while 50 patients (26.2%) had a Ki-67 index <20%. No statistically significant association was found between Ki-67 index and luminal subtype (p-value=0.383). A higher proliferative index was observed in Luminal A and Basal-like subtypes, both of which were HER2-negative. However, other studies have reported higher Ki-67 expression in HER2-positive tumours [21,22].

Among Basal-like tumours, 21.5% showed a high proliferative index. These triple-negative breast cancers are known for their aggressive behaviour and poor prognosis, despite good responsiveness to chemotherapy [23]. The presence of a low-proliferative Basal-like subgroup suggests biological heterogeneity within this category.

No statistically significant association was found between age and luminal subtype (p-value=0.983). Although older women tend to present more frequently with Luminal A tumours and younger women with aggressive subtypes [24], this trend was not statistically significant in the present study. Therefore, age alone may not be a reliable prognostic factor when molecular subtypes are considered [24].

Limitation(s)

The quality and consistency of IHC were not uniform, as reports were obtained from multiple laboratories using different antibodies and reporting protocols. A standardised molecular analysis with strict quality control from a single laboratory would have provided more reliable insights.

CONCLUSION(S)

The present study demonstrated that the Luminal A subtype was the most prevalent, followed by Basal-like, Luminal B, and HER2-enriched subtypes in this specific geographical region. The findings highlight that BC molecular subtypes vary with age, ethnicity, and demographic factors. Such data are crucial for prognostication and individualised treatment planning. Additionally, region-specific epidemiological data can aid healthcare policymakers in optimising resource allocation for diagnostic and therapeutic services, particularly in publicly funded healthcare institutions, ultimately contributing to improved BC survival outcomes.

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PARTICULARS OF CONTRIBUTORS:

- Senior Assistant Professor, Department of Radiation Oncology, Government Villupuram Medical College and Hospital, Villupuram, Tamil Nadu, India.
- Assistant Professor, Department of Pathology, Government Medical College, Kallakurichi, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Rajiv Kumar Krishnan,
Senior Assistant Professor, Department of Radiation Oncology, Government Villupuram Medical College and Hospital, Mundiampakkam-605601, Villupuram, Tamil Nadu, India.
E-mail: ungalrajiv@gmail.com

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