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Molecular subtyping of breast carcinomas in urban and rural Indian population – A cross-sectional study.

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Abstract

Background

Consequently, one crucial aspect for the treatment profile of breast cancer is the classification of breast cancer into pertinent molecular subgroups. Breast cancer is divided into four primary clinical subtypes based on gene expression profiles, receptor status, and proliferative status. There hasn't been much research done on how common these molecular subtypes are among Indian people.

Objectives

The purpose of conducting this analysis was to evaluate the molecular subtyping of breast cancer in Indians living in both urban and rural areas.

Materials and Methods

It was a prospective, observational study. The study was carried out in SCB Medical College & Hospital, Odisha, India. The study was conducted for two years, that is, from January 2023 to April 2025. In all, 150 patients were enrolled. Study participants included all females with breast cancer.

Results

With 83 (55.3%) patients older than 50, the mean age at diagnosis was skewed toward older patients. Metastases from lymph nodes were found in 89 patients, or 59.3%. In 32 (21.3%) of the cases, distant metastases were discovered at the time of initial presentation. Of the population, 24 (16.0%) had luminal A-like tumors.

Conclusion

This study uses immunohistochemistry surrogate markers to show the distribution of subtypes that are molecular in breast cancer in an Indian population living in both urban and rural areas. The majority of patients come with high-grade tumors and substantial nodal involvement, and the results show a preponderance of aggressive subtypes, including TNBC and Luminal B-like cancers.

Recommendation

Routine molecular subtyping using immunohistochemistry should be incorporated into the diagnostic evaluation of all invasive breast cancer cases to guide treatment decisions effectively.

Keywords: *Triple-negative breast tumors, Human Epidermal Growth Factor Receptor 2 (HER2), breast cancer, Molecular subtyping, Triple-Negative Breast Cancer (TNBC).*
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Introduction

In almost all cases of women having breast cancer, it is the most prevalent cancer worldwide [1]. North America, Europe, and Australia have the highest rates of breast cancer.

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Recent evidence indicates that the rates of mortality among cancer are declining, even though it is still the top cause of cancer death in women [2].

Increased awareness, screening initiatives, and improvements in focused treatment are to blame for this. According to gene expression research, the intrinsic molecular features of the tumor, not morphological prognostic markers, are the primary determinants of the tumor's response to treatment. With the development of high-throughput platforms for gene expression investigation, like microarrays, these intrinsic molecular characteristics can be investigated utilizing molecular techniques [3].

Consequently, one crucial aspect for the treatment profile of breast cancer is the classification of breast cancer into pertinent molecular subgroups. Breast cancer is divided into four primary clinical subtypes based on gene expression profiles, status of receptor, and status that is proliferative as determined by Ki67, estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) [4].

Luminal A, luminal B, HER2-enriched, and triple-negative breast tumors (TNBC) are some of these clinical subgroups. The chance of an early recurrence is higher for breast tumors that are not luminal A. TNBCs are aggressive, showing advanced illness and a higher histological grade.

Over the past few decades, the incidence of breast cancer has been steadily rising, with Asian countries seeing the biggest increases. With an overall change in incidence of roughly 0.4–0.6, breast cancer has become the most frequent cancer in women in India over the past 20 years [5].

The profiling of gene expressions is not widely used in ordinary clinical practice because of issues of cost and complexity observed technically. Cheang et al. proposed a more useful immunohistochemistry surrogate categorization [6].

There hasn't been much research done on how common these molecular subtypes are among Indian people. The purpose of conducting this study was to evaluate the molecular subtyping of breast cancer in Indians living in both urban and rural areas.

Methodology

Study Design

This was a prospective, cross-sectional observational study conducted to assess receptor status in patients with invasive breast cancer.

Study Setting

The study was conducted at SCB Medical College & Hospital, Odisha, India, over two years, from January 2023 to April 2025.

Study Population

A total of 150 female patients diagnosed with invasive breast cancer were enrolled in the study.

Inclusion Criteria

- Female patients diagnosed with invasive breast cancer.
- Patients who underwent reflex fluorescence in situ hybridization (FISH) testing, when indicated.
- Patients with complete receptor status data (ER/PR/HER2).

Exclusion Criteria

- Patients without reflex FISH testing.
- Patients with bilateral breast cancer (either synchronous or metachronous).
- Patients with missing receptor status data (ER/PR/HER2).

Data Collection

Information about the pathology results and baseline clinical features of the selected cases was gathered from the electronic medical records. Age at diagnosis, tumor size,

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histological subtype, and tumor grade were among the parameters evaluated. The radiographic size of the tumor before neoadjuvant chemotherapy (NACT) was taken into account in patients who had surgery.

Study Procedure

Immunohistochemistry (IHC) slides that were stained were used to undergo processing for the identification of receptors. Also, the cases with unclear HER2 staining were forwarded to FISH for additional analysis, and the outcomes were recorded. The study did not include cases where FISH testing was not possible.

Bias

To minimize selection bias, consecutive sampling was employed for all eligible patients meeting the inclusion criteria. Data extraction followed standardized procedures by trained personnel to reduce information bias.

Statistical Analysis

Data were initially entered in Microsoft Excel. The data has been presented as the number of participants (n) and percentages (%).

Ethical Clearance

Informed consent was taken from all participants.

Results

A total of 180 patients with invasive breast cancer were initially screened for eligibility during the study period. Following the initial screening, 165 patients were examined for eligibility. Among these, 15 patients were excluded due to the following reasons: lack of reflex fluorescence in-situ hybridization (FISH) testing in 6 patients, presence of bilateral breast cancer (either synchronous or metachronous) in 5 patients, and incomplete receptor status data in 4 patients. Consequently, 150 patients were confirmed eligible, enrolled in the study, and all participants completed follow-up and were included in the final analysis.

The clinicopathological profile of patients with breast cancer is displayed in Table 1 according to age and tumor features. With 83 (55.3%) patients older than 50, the mean age at diagnosis was skewed toward older patients. Metastases from lymph nodes were found in 89 patients, or 59.3%. In 32 (21.3%) of the cases, distant metastases were discovered at the time of initial presentation.

Table 1. Clinicopathological Profile of Breast Carcinoma Patients Based on Tumor Characteristics and Age

Parameters	Number of Participants (n)	Percentages (%)
Size of Tumor		
≤ 2.0 cm	15	10.0%
> 2.0 – 5.0 cm	95	63.3%
> 5.0 cm	40	26.7%
Tumor Grade		
Grade I	01	0.7%
Grade II	36	24.0%
Grade III	113	75.3%
Age at Diagnosis		
≤ 50 years	67	44.7%
> 50 years	83	55.3%
Distant Metastasis at Diagnosis	32	21.3%
Lymph Node Metastasis	89	59.3%

The Luminal B-like subtype, which accounted for 42.0% of cases overall and was further subdivided into Her2-negative 36 (24.0%) and Her2-positive 27 (18.0%) categories, was the next most prevalent group. Of the population, 24 (16.0%) had luminal A-like tumors. The distribution of

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subtypes of molecular receptors in cancer of breast is shown in Table 2

Table 2. Distribution of Molecular Subtypes of Breast Cancer

Molecular Subtype	Number of Patients (n)	Percentage (%)
Triple Negative (TNBC)	40	27.0%
Luminal A-like	24	16.0%
Luminal B-like (Her2-negative)	36	24.0%
Luminal B-like (Her2-positive)	27	18.0%
Her2-positive (non-luminal)	23	15.0%

Discussion

The study shows subtypes of molecular receptors among participants with breast cancer. The average age of all the included participants was found to be 55 years, which is comparable to earlier studies conducted in India but around ten years younger than the average age in the Western population [7]. A small percentage of patients (n = 30, 1.84%) presented at a younger age (≤30 years). However, a different study found that 10% of the participants were young people with breast cancer [8].

Compared to data reported in the western community, our research population's patients had more frequent nodal involvement and higher tumor sizes at presentation [7]. Due to the absence of a screening program, many women who cannot afford the proper testing lack a diagnosis on time, which further leads to ignorance of breast cancer.

According to the majority of Indian studies, 50–60% of malignancies are ER/PR positive [8, 9, 10]. However, this is less than the ER/PR positive found in other investigations conducted in the West [7]. This discrepancy can be explained by the various epidemiological characteristics of the Indian population, and it has been observed that many participants suffer from high-grade cancer while they are young [11].

Thirty-three percent of the study participants had HER2-positive. This finding is consistent with the published Indian literature, which reports that between 20 and 30 percent of breast tumors are HER2 positive [8, 9, 10]. According to subanalyses of the luminal B-like (HER2-negative) and luminal A-like subtypes, luminal B-like (HER2-negative) cancers were more likely to have node-negative disease and a lower tumor grade than luminal A-like tumors. These results are consistent with prior research [12, 13].

In another study, Prat et al reported that positivity of PR more than 20% determines the luminal A types of tumors through the processing of IHC. The conclusion that a poorer prognosis for luminal tumors is linked to low or negative PR expression served as the basis for this [14].

In the current analysis, the least prevalent molecular subtype was the HER2-positive (non-luminal) subtype. Similar results were also observed by Kunheri et al. in their study [13]. As the tumors were categorized equally, it was considered the main strength of the respective study.

Conclusion

This study uses immunohistochemistry surrogate markers to show the distribution of subtypes that are molecular in breast cancer in an Indian population living in both urban and rural areas. The majority of patients come with high-grade tumors and substantial nodal involvement, and the results show a preponderance of aggressive subtypes, including TNBC and Luminal B-like cancers. These findings highlight the value of early detection and the necessity of economical molecular subtyping in directing treatment choices, especially in environments with limited resources.

Limitations

There are a couple of significant drawbacks to this study, though. One of the limitations was the small number of patients, which might affect the efficiency and the duration of time.

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Recommendations

Further research, including larger-scale studies, is necessary to validate these observations and enhance our understanding of the role of molecular subtypes in assessing breast carcinoma. Improving results in this population requires expanding access to diagnostic and focused treatment approaches.

List of Abbreviations

ER- Estrogen receptor
PR- Progesterone receptor
HER 2- Human epidermal growth factor receptor 2
TNBC- Triple-negative breast cancers
FISH- Fluorescence in-situ hybridization
NACT- Neoadjuvant chemotherapy
IHC- Immunohistochemistry

Generalizability

The findings of this study are applicable to breast cancer patients attending tertiary care centers in India with similar clinical settings. However, the results may not be fully generalizable to rural populations or other regions with differing healthcare access.

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Source of Funding

This study did not receive any external funding and was fully self-supported by the investigators.

Conflict of Interest

The authors declare that there are no conflicts of interest related to this study.

Availability of Data

Data generated or analysed during this study are available from the corresponding author upon reasonable request.

Authors' Contribution

All authors contributed to study design and manuscript preparation. Data collection and analysis were primarily performed by the first author, with all authors reviewing and approving the final manuscript.

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