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MOLECULAR PROFILING OF BREAST CANCER AND ITS IMPLICATIONS FOR TARGETED THERAPY IN TERTIARY CARE CENTRES IN EASTERN UTTAR PRADESH, INDIA

General Surgery

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ABSTRACT

Breast cancer is a primary contributor to the death toll from cancer in women worldwide. The problem exhibits significant heterogeneity in its molecular and clinicopathological characteristics. The present study uncovers the molecular subtypes of breast cancer in patients from a tertiary care centre in Eastern Uttar Pradesh, India and investigates the potential impact of these subtypes on targeted therapy. By conducting a meticulous examination of hormone receptor status and HER2 expression, the study reveals patterns that provide insights into approaches to treatment and enhance patients' overall results. The findings reveal a predominance of A+B subtype and significant relationships between hormone receptor status and clinical stage that highlights the importance of molecular profiling in guiding targeted therapies.

KEYWORDS

Breast cancer, molecular profile, clinicopathological characteristics, Eastern Uttar Pradesh, hormone receptors

INTRODUCTION

Breast cancer is a complex ailment distinguished by several molecular subtypes, each having unique consequences for prognosis and treatment. The introduction of molecular profiling has significantly transformed the comprehension and control of breast cancer, enabling the development of more meticulous and refined therapeutic approaches (Perou et al., 2000). The categorisation of breast cancer into several subtypes, such as luminal A, luminal B, HER2-enriched, and triple-negative breast cancer (TNBC), has been made possible by recent advancements in molecular biology, namely through the analysis of gene expression patterns (Sørlie et al., 2001). These subgroups exhibit variations in their biological characteristics, responsiveness to treatment, and clinical results, hence requiring the implementation of advanced therapeutic strategies. The investigation of molecular profiling in breast cancer has predominantly concentrated on Western populations, with few data accessible from emerging nations like India. It is crucial to investigate the molecular and clinicopathological features of breast cancer in Indian women due to the distinct genetic and environmental variables that influence the illness in this community (Saxena et al., 2012). This study aims to fill this void by examining breast cancer patients in a tertiary care centre in Eastern Uttar Pradesh. The primary focus will be on analysing the hormone receptor status, HER2 expression, and their relationship with clinical characteristics.

MATERIALS AND METHODS

Study Design and Population

This study was conducted for 1 year at the B.R.D Medical College, Gorakhpur, a tertiary care centre in Eastern Uttar Pradesh, India. The study included 50 breast cancer patients diagnosed and treated from 2023-2024.

Sample Size:

Fifty patients were enrolled based on the formula:

$=4pq/d^2$

where p is prevalence, q is 1−p, and d is the absolute error.

The inclusion criteria were histologically confirmed invasive breast cancer and availability of complete clinicopathological and molecular data. Patients with incomplete records or previous cancer diagnoses were excluded.

Data Collection

Method of Study:

For Histopathological Examination, tissue specimens were fixed in 10% formalin, embedded in paraffin, sectioned, and stained with Hematoxylin and Eosin (H&E). Clinical data, including age, menopausal status, tumor size, lymph node involvement, and stage at diagnosis, were extracted from medical records. Molecular profiling data that includes estrogen receptor (ER), progesterone receptor (PR), and HER2 status, were obtained from immunohistochemistry (IHC) reports. The IHC results were interpreted using the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines.

Statistical Analysis

Descriptive statistics were used to summarize the demographic and clinicopathological characteristics of the study population. The chi-square test was employed to assess associations between molecular subtypes and clinical features. A p-value of <0.05 was considered statistically significant. All analyses were performed using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA).

RESULTS AND DISCUSSION

Demographic and Clinical Characteristics:

A total of 50 breast cancer patients were included in the study, with a mean age of 48.4 years (range: 25-75 years) (Table 1). Notably, all participants reported no family history of breast cancer. The majority had no history of oral contraceptive pill usage, and all participants had no history of hormone replacement therapy. 52% of patients were premenopausal that highlights the relatively younger age of onset in this population compared to Western countries (Porter, 2008). The most common tumor stage at diagnosis was stage II (56%), followed by stage III (30%), stage I (14%), and stage IV (0%). (Fig. 1)

Table 1: Demographic and Clinical Characteristics

Characteristic	Value
Total Number of Patients	50
Mean Age	48.4 years
Age Range	25-75 years
Percentage of Premenopausal Patients	52%

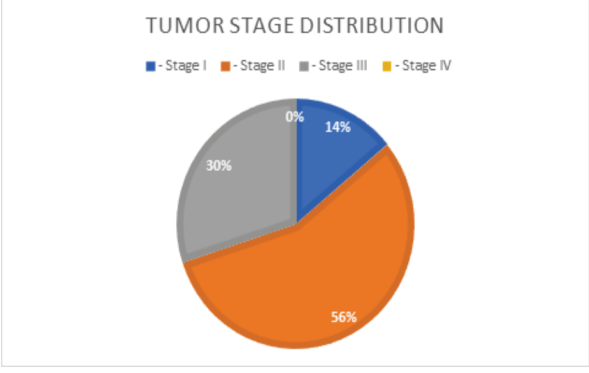

Fig. 1 Distribution of Patients Across Tumor Stages in the Study Population

The analysis revealed a predominance of hormone receptor-positive (HR+) subtypes. Among the cases, 62.00% of the total were negative for HER2 Enriched, while 38% were positive for HER2 Enriched. This finding aligns with previous studies that have reported a high prevalence of HR+ breast cancer in Indian women (Chopra et al., 2018). HER2-positive cases constituted 25% of the study population, while triple-negative breast cancer (TNBC) accounted for 15%.

Table 2: The Distribution of Molecular Subtype

Molecular Subtype	Counts	Percentage (%)
Luminal A+B	36	72 %
HER2-Enriched	11	22 %
Triple-Negative Breast Cancer (TNBC)	3	6 %

Molecular Subtypes and Clinical Correlations:

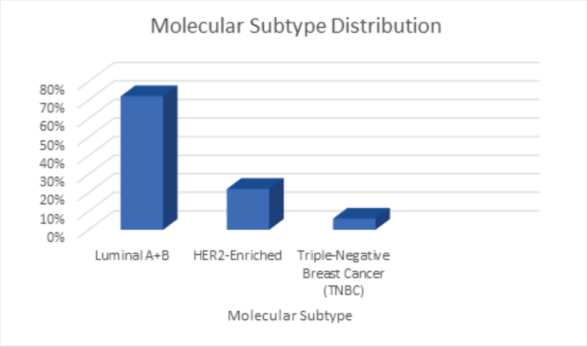

Fig. 2 Distribution of Breast Cancer Molecular Subtypes

The molecular subtypes in the study population were distributed as follows: A+B (72.00%), HER2-enriched (22.00%), and TNBC (6.00%). The cumulative percentage approaches 100.00% with the inclusion of all categories (Fig. 2).

The Luminal A and B are the most common in the early phases of cancer. The high predominance of luminal A tumours, which are characterised by strong ER/PR expression and slow proliferation rates. This indicates a good prognosis and response to endocrine treatment (Goldhirsch et al., 2011).

In contrast, HER2-enriched subtypes are less common yet present throughout stages I to III, which pictures the aggressive character of HER2-positive malignancy. It is frequently detected at an advanced stage.

HER2-enriched tumours were related with greater tumour size, higher histological grade, and increased lymph node involvement, which is consistent with their aggressive clinical behaviour (Gianni et al. 2011). The inverse correlation between ER and HER2-enriched subtypes highlights the unique molecular pathways that underpin these subtypes (Pusztai et al., 2006). Targeted medicines such as trastuzumab and lapatinib have demonstrated success in HER2-positive breast cancer, emphasising the necessity of precise molecular characterisation.

The correlation analysis revealed significant relationships between ER and HER2 Enriched ($p = 0.006$), PR and ER ($p < 0.001$), and PR and HER2 Enriched ($p = 0.019$), while PR, menopausal status, and molecular subtypes, were non-significant with p-values greater than 0.05 .

TNBC with no expression of ER, PR, or HER2 was related with poor differentiation, high proliferation rates, and early recurrence. The lack of targeted therapeutics for TNBC underscores the need for new treatment strategies, such as PARP inhibitors and immunotherapy (Bianchini et al., 2016). The study's findings highlight the significance of molecular profiling in influencing treatment decisions and improving patient outcomes.

Implications for Targeted Therapy:

The identification of molecular subtypes has important implications for the treatment of breast cancer in the study population. Endocrine treatment with tamoxifen or aromatase inhibitors benefits hormone receptor-positive tumours, particularly luminal A, by lowering the risk of recurrence and enhancing survival (Early Breast Cancer Trialists' Collaborative Group, 2011). HER2-positive patients, who make about 25% of cases, may benefit from HER2-targeted therapy, which have considerably improved outcomes in this aggressive subtype (Hudis,2007).

The issue continues in properly treating TNBC, which has no specific treatments. Recent advances in understanding the molecular causes of TNBC have resulted in the development of new medicines like as immune checkpoint inhibitors and PARP inhibitors, which provide promise for better results in this difficult subtype (Tutt et al., 2021). The report emphasises the importance of continuous research and clinical trials to develop viable therapies for TNBC and other aggressive subtypes.

CONCLUSION

Molecular profiling provides valuable insights into the heterogeneity of breast cancer that allows for more personalized and effective treatment strategies. This study highlights the distribution of molecular subtypes in a tertiary care center in Eastern Uttar Pradesh and their correlation with clinicopathological features. The findings emphasize the importance of regular molecular characterization in guiding treatment decisions and improving patient outcomes.

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