Section: General Surgery

Original Research Article

CLINICO-EPIDEMIOLOGICAL STUDY OF BREAST CARCINOMA AND CO RELATION OF EXPRESSION OF ER (ESTROGEN RECEPTOR), PR (PROGESTERONE RECEPTOR), HER-2NEU (HUMAN EPIDERMAL GROWTH RECEPTOR 2) RECEPTOR STATUS WITH KI-67 INDEX IN KUMAON REGION OF UTTARAKHAND

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Abstract

Background: Breast carcinoma is a leading malignancy among women worldwide, characterized by diverse clinical and molecular profiles influencing prognosis and treatment outcomes. This clinico-epidemiological study focuses on the Kumaon region of Uttarakhand, examining the correlation between receptor status—Estrogen Receptor (ER), Progesterone Receptor (PR), and Human Epidermal Growth Factor Receptor 2 (HER-2/neu)—and the Ki-67 proliferation index in breast cancer patients. A total of 150 histopathologically confirmed cases of breast carcinoma were analyzed for demographic patterns, clinical presentation, and receptor status using immunohistochemistry. The study found that the majority of patients were in the 40–60 age group, with invasive ductal carcinoma being the predominant histological type. ER and PR positivity was observed in 55% of cases, indicating hormone receptor sensitivity, while HER-2/neu positivity was noted in 25% of cases. Triple-negative breast cancer accounted for 15%, typically presenting with aggressive clinical behavior. The Ki-67 index varied significantly across subtypes, with higher values correlating with HER-2/neu positivity and triple-negative status, reflecting their higher proliferative activity and poor prognosis. A significant association was observed between receptor status and Ki-67 index, aiding in categorizing tumors into distinct molecular subtypes—luminal A, luminal B, HER-2/neu enriched, and triple-negative. This stratification has implications for personalized treatment strategies, particularly in selecting targeted therapies such as hormonal agents or HER-2/neu inhibitors. The study highlights the importance of Ki-67 as a prognostic marker and its role in guiding therapeutic decisions. This research provides valuable insights into the molecular and epidemiological landscape of breast cancer in the Kumaon region, emphasizing the need for routine receptor and Ki-67 evaluation to optimize treatment outcomes and enhance patient care. Future studies are warranted to explore long-term survival outcomes and therapeutic efficacy.

INTRODUCTION

Breast cancer is the most prevalent cancer among women globally and the leading cause of cancer-related deaths. In regions like Iran and India, the disease exhibits significant biological heterogeneity.[1] Recent years have seen a focus on molecular markers such as estrogen receptor (ER), progesterone receptor (PR), HER2/neu, Ki-67, and p53 through immunohistochemistry (IHC) to predict disease outcomes and guide treatment decisions. Hormone receptor status, particularly ER and PR, serves as a key prognostic indicator, providing insights into the likelihood of response to endocrine therapies like tamoxifen. Tumors positive for ER and PR are associated with better prognosis and therapeutic responsiveness compared to hormone receptor-negative tumors.[2]

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HER2/neu, a proto-oncogene located on chromosome 17q21, encodes a growth factor receptor linked to tumor proliferation. HER2 overexpression is observed in 15-30% of breast cancers and is often associated with poor prognosis, recurrence, and resistance to hormonal therapies.[3] However, targeted therapies like trastuzumab have improved outcomes for HER2-positive patients.[4] The Ki-67 proliferation index has emerged as a vital marker, correlating with higher histological grades, larger tumors, lymph node metastases, and reduced survival rates. Elevated Ki-67 levels indicate aggressive disease behavior and serve as a predictor of treatment outcomes.[5]

In India, breast cancer incidence is increasing, surpassing cervical cancer in urban areas such as Mumbai, Delhi, and Chennai. Histopathological examination remains the cornerstone for diagnosis, with IHC playing a pivotal role in categorizing tumors based on molecular markers. Despite advancements in molecular testing, accessibility and cost remain significant barriers in low-resource settings.[6] IHC provides a cost-effective and accessible alternative, offering both therapeutic and prognostic insights.[7]

Studies demonstrate that ER and PR expression varies with tumor grade and histology, with nearly all grade I tumors showing ER positivity. HER2 overexpression has been linked to adverse outcomes, particularly in lymph node-positive patients. Combining ER, PR, and HER2 status has proven valuable for molecular classification, aiding in clinical evaluation and treatment planning.[8]

Recent advancements in breast cancer management have enabled early detection and more effective treatments, leading to improved survival rates. However, racial and demographic factors influence immune responses and disease characteristics, emphasizing the need for localized research.[9] In the Kumaon region of Uttarakhand, breast cancer trends and their correlation with molecular markers like ER, PR, HER2, and Ki-67 are crucial for personalized treatment strategies.[10]

This study aims to analyze the expression of these markers and their relationship with clinical and epidemiological parameters in breast cancer patients from the Kumaon region. Findings from this research could enhance understanding of disease biology, facilitate tailored treatment approaches, and improve outcomes for patients in this specific demographic.[11]

MATERIALS AND METHODS

A cross-sectional study was conducted in the Department of General Surgery, Government Medical College, and Dr. Susheela Tiwari Government Hospital, Haldwani, Uttarakhand, over 18 months. An ethical approval has been obtained from the Ethical Approval Committee. Thirty-one patients were purposively sampled based on inclusion criteria, including consent and undergoing biopsies or mastectomy. Excluded were those unwilling to participate. Detailed histories, clinical examinations, and diagnostic evaluations (FNAC, mammography, and molecular markers like ER, PR, and HER2/neu) were performed. Molecular subtypes (luminal A/B, HER2, and triple-negative) were correlated with IHC biomarkers. Written informed consent was obtained, and demographic data recorded, facilitating population-based research using cancer registry data.

RESULTS

The study included 62 participants with a mean age of 50.79±11.51 years. Most were aged 35-50 years (51.6%), followed by 50-65 years (43.5%). Only 3.22% were under 30, and 1.6% were over 65. Statistical analysis yielded a p-value of 1.231, indicating no significant age group differences. [Table 1]

The study of 62 breast carcinoma patients revealed a predominance of females (96.8%), with males comprising only 3.2%. Despite this disparity, the p-value indicated no significant gender difference. These findings emphasize that breast carcinoma predominantly affects females in the studied population. [Table 2]

Among 62 breast carcinoma patients, only 8.1% reported a familial history of carcinoma, while 91.9% had no such history. The p-value of 0.001 indicated a statistically significant difference in this distribution, suggesting that a familial history of carcinoma was relatively uncommon in the study population. [Table 3]

Among 62 breast carcinoma patients, 98.4% had invasive ductal carcinoma, while 1.6% had fibroadenoma. The p-value indicated no significant difference in histopathological type distribution, emphasizing invasive ductal carcinoma as the predominant type in the study population. [Table 4]

Among 62 breast carcinoma patients, 58.1% were postmenopausal, 38.7% premenopausal, and 3.2% had unknown menstrual status. The p-value of 0.003 showed a significant difference, highlighting a higher prevalence of breast carcinoma in postmenopausal women within the study population. [Table 5]

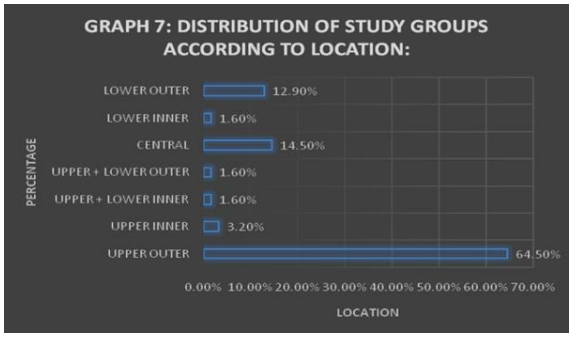

Figure 1: distribution of study groups according to location

Among 62 breast carcinoma patients, 85.5% showed no clinical axillary lymph node involvement, while

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14.5% had lymph nodes involved. A p-value of 0.002 indicated a significant difference, emphasizing that most patients lacked clinical axillary lymph node involvement. [Table 6]

In a study of 62 breast carcinoma patients, the upper outer quadrant was the most common tumor site (64.5%), followed by the central location (14.5%) and lower outer quadrant (12.9%). Other locations accounted for minimal cases. A p-value of 1.001 indicated no significant difference in tumor location distribution, highlighting the upper outer quadrant's predominance.

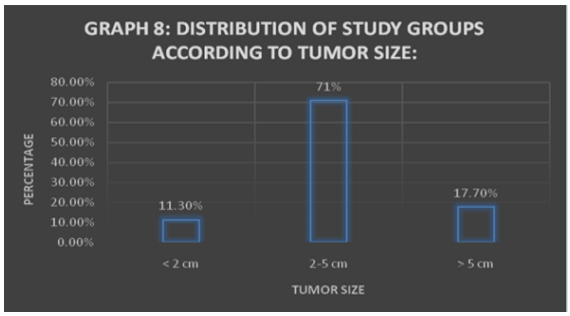

Figure 2: distribution of study groups according to tumor size

In the study of 62 breast carcinoma patients, 71% had tumors sized between 2-5 cm, 17.7% had tumors larger than 5 cm, and 11.3% had tumors smaller than 2 cm. A p-value of 0.551 indicated no significant difference in tumor size distribution, with the most common tumor size being 2-5 cm.

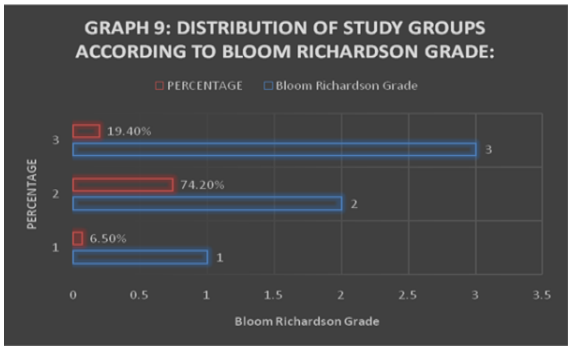

Figure 3: distribution of study groups according to bloom richardson grade

In the study of 62 breast carcinoma patients, 74.2% had grade 2 tumors, 19.4% had grade 3, and 6.5% had grade 1 tumors. A p-value of 0.004 indicated a significant difference in grade distribution. These results highlight that grade 2 was the most prevalent Bloom Richardson grade in the study population.

The study of 62 breast carcinoma patients found that 56.5% were estrogen receptor (ER)-negative, while 43.5% were ER-positive. A p-value of 0.0011 indicated a statistically significant difference in ER status distribution. These findings suggest that ER-negative cases were more prevalent than ER-positive cases in the study population.

The study of 62 breast carcinoma patients found that 58.1% were progesterone receptor (PR)-negative, while 41.9% were PR-positive. A p-value of 0.02 indicated a statistically significant difference in the distribution of PR status. These results suggest that PR-negative cases were more common than PR-positive cases in the study population.

The study of 62 breast carcinoma patients found that 74.2% were HER-2/neu-negative, 24.2% were HER-2/neu-positive, and 1.6% had an equivocal result. A p-value of 0.741 indicated no significant difference in the distribution of HER-2/neu status. These results suggest that most breast carcinoma cases in the study were HER-2/neu-negative.

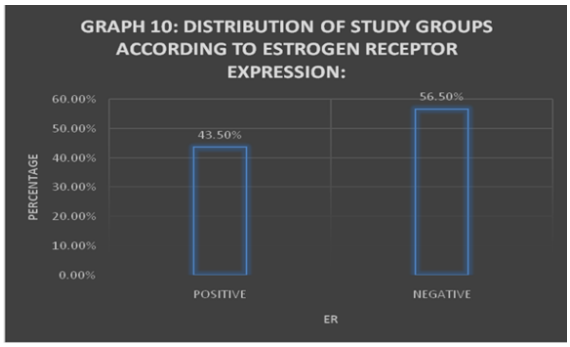

Figure 4: distribution of study groups according to estrogen receptor expression

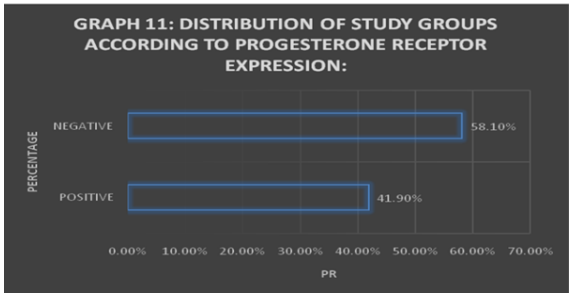

Figure 5: distribution of study groups according to progesterone receptor expression

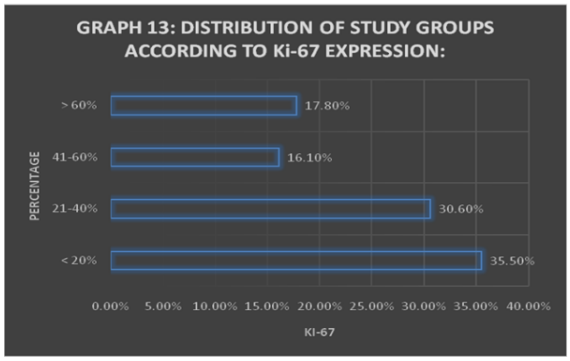

Figure 6: distribution of study groups according to ki-67 expression

The study of 62 breast carcinoma patients found varying Ki-67 proliferation indices: 35.5% had less than 20%, 30.6% had 21-40%, 16.1% had 41-60%, and 17.8% had more than 60%. A p-value of 0.001 indicated a significant difference in Ki-67 distribution. These findings suggest a diverse Ki-67 index, with most patients showing a Ki-67 index of less than 20%.

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Table 1: distribution of study groups according to age groups.

Age groups	Frequency	Percentage	P-value
< 30	2	3.22%	1.231
35-50	32	51.60%	
50-65	27	43.50%	
> 65	1	1.60%	
TOTAL	62	100	
MEAN + SD	50.79±11.51		

Table 2: distribution of study groups according to gender

Gender	Frequency	Percentage	P-value
Male	2	3.2	
Female	60	96.8	
Total	62	100.0	

Table 3: distribution of study groups according to family history of carcinoma

Familial h/o carcinoma	Frequency	Percentage	P-value
Yes	5	8.1%	0.001
No	57	91.9%	
Total	62		

Table 4: distribution of study groups according to histopathology report

Histopathology report	Frequency	Percentage	P-value
Invasive ductal carcinoma	61	98.4%	
Fibroadenoma	1	1.6%	
Total	62	100.0	

Table 5: distribution of study groups according to menstrual status

Menstrual status	Frequency	Percentage	P-value
Pre	24	38.7%	0.003
Post	36	58.1%	
Na	2	3.2%	
Total	62	100.0	

Table 6: distribution of study groups according to axillary lymph node status (clinical)

Axillary lymph node status	Frequency	Percentage	P-value
Absent	53	85.5%	0.002
Present	9	14.5%	
Total	62		

Table 7: distribution of study groups according to her-2-neu expression

Her-2-neu	Frequency	Percentage	P-value
Positive	15	24.2%	0.741
Negative	46	74.2%	
Equivocal	1	1.6%	
Total	62		

DISCUSSION

Breast cancer remains a leading cause of illness and death among women worldwide, with metastasis occurring in 5-10% of patients at diagnosis. Metastatic breast cancer generally has a poor prognosis, with a 5-year survival rate of around 25%. For early-stage breast cancer patients who receive adjuvant therapy, 20-30% will eventually develop metastatic disease.[12] Common sites of metastasis include the bone, lung, and pleura, with median survival following metastasis ranging from 0.5 to 3 years.[13] Treatment strategies often depend on the molecular classification of the cancer, which involves markers such as estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER-2), and Ki-67 index, which are essential for determining prognosis and therapeutic approaches.[14]

The estrogen receptor (ER) is particularly significant in breast cancer prognosis and treatment response. A combination of positive ER and progesterone receptor (PgR) is associated with a better prognosis and increased sensitivity to hormone therapy. Molecular subtypes based on receptor status can guide therapy, with ER-negative and PgR-positive cancers showing different treatment responses compared to ER-positive tumors. The classification of breast cancer based on these markers is crucial for selecting the right treatment regimen for each patient.[15]

A study conducted in the Kumaon region aimed to explore the relationship between these molecular markers (ER, PR, HER-2, and Ki-67) and clinico-epidemiological characteristics of breast cancer. It was a cross-sectional study, which involved 62 patients who underwent various procedures like mastectomy and biopsies over an 18-month

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period.[16] The study found that breast cancer was most prevalent in women between 35-50 years of age, comprising 51.6% of the sample. The next largest group was aged 50-65 years (43.5%). The study did not show a significant variation in age distribution across different groups, with the average age of patients being 50.79 years. This age distribution mirrors findings in other studies, where breast cancer in younger women is often associated with more advanced stages of the disease.[17]

Gender distribution showed that 96.8% of breast cancer patients were women, with only 3.2% being men. Male breast cancer is rare, accounting for less than 1% of cases.[18] A familial history of breast cancer was present in just 8.1% of the patients, which is consistent with findings from other studies, suggesting that most cases of breast cancer occur without a significant family history. Histologically, invasive ductal carcinoma was the most common type, accounting for 98.4% of cases, with only 1.6% diagnosed with fibroadenoma.[19] The menstrual status of patients revealed that 58.1% were postmenopausal, 38.7% were premenopausal, and 3.2% had uncertain menstrual status. The study found that postmenopausal women had a higher incidence of breast cancer, which has been noted in other studies as well. However, some research suggests that menstrual status may not significantly affect the prognosis of breast cancer.[20]

In terms of axillary lymph node involvement, 85.5% of patients were free from lymph node metastasis, while 14.5% showed involvement. This finding is in line with other studies that suggest the presence of axillary lymph node metastasis is associated with a worse prognosis. Regarding tumor location, the upper outer quadrant of the breast was the most common site for tumors, accounting for 64.5% of cases.[21] This is consistent with other studies that have noted that tumors located in the central or inner quadrants tend to have a worse prognosis due to their larger size.[22]

The study also evaluated tumor size and grade. The majority of tumors were between 2-5 cm (71%), with only a small proportion being larger than 5 cm or smaller than 2 cm.[23] The Bloom Richardson grade revealed that most tumors were grade 2 (74.2%), followed by grade 3 (19.4%) and grade 1 (6.5%). This grading system is widely used for assessing breast cancer severity and prognosis, and the findings here reflect typical distribution patterns.[24]

The ER status in the study sample showed that 56.5% of patients were ER-negative and 43.5% were ER-positive. This suggests a higher prevalence of ER-negative breast cancer in the Kumaon region, which is associated with a more aggressive form of the disease and poorer prognosis. The study also found that 58.1% of patients had a negative progesterone receptor (PR) status, and 41.9% were PR-positive.[25] The differences in PR status were statistically significant, indicating that PR status may also play a role in determining treatment strategies and outcomes.[26]

Overall, this study provides valuable insights into the clinico-epidemiological characteristics of breast cancer in the Kumaon region. The findings emphasize the importance of molecular markers like ER, PR, HER-2, and Ki-67 in guiding treatment decisions, as well as highlighting the demographic and histological patterns observed in this cohort.[27]

CONCLUSION

This cross-sectional study examined breast carcinoma in the Kumaon region, involving 62 patients. It found that most patients were aged 35-65, with invasive ductal carcinoma being the predominant type. Postmenopausal women had a higher incidence, and tumors were mainly located in the upper outer quadrant, ranging from 2-5 cm in size. The study highlighted significant findings, including higher rates of ER-negative, PR-negative, and HER-2/neu-negative statuses. Luminal A was the most common molecular subtype. Statistically significant associations were found with age, gender, menstrual status, tumor size, lymph node involvement, and receptor status, emphasizing the need for targeted treatments.

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