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Evaluation Of Hormone Receptors And Ki-67 In Tumor And Peritumoral Region Of Breast Carcinoma

Yazhini V[1], Kavithamani K[2], Bhavani K[3], Sowmya S[4], Rajan K.V[5]

[1]Postgraduate, Department of Pathology, Mahatma Gandhi Medical college and research Institute, Sri Balaji Vidyapeeth (deemed to be university) ,Pondicherry, India

Email id: yazhinivenkat13@gmail.com

[2]Assistant Professor, Department of Pathology, Mahatma Gandhi Medical college and research Institute, Sri Balaji Vidyapeeth (deemed to be university) Pondicherry, India.

Email id: drkavithalokesh@gmail.com

[3]Professor, Department of Pathology, Mahatma Gandhi Medical college and research Institute, Sri Balaji Vidyapeeth (deemed to be university)Pondicherry, India

[4]Professor & Head, Department of Pathology, Mahatma Gandhi Medical college and research Institute, Sri Balaji Vidyapeeth (deemed to be university) Pondicherry, India

Email id: drssowmya@hotmail.com

[5]Professor, Department of General Surgery, Mahatma Gandhi Medical college and research Institute, Sri Balaji Vidyapeeth (deemed to be university) Pondicherry, India

Email id: rajankv@mgmcri.ac.in

Corresponding author:

Dr. Kavithamani K

Email id : drkavithalokesh@gmail.com

ABSTRACT

Background: Hormonal receptors and proliferative indices such as estrogen receptor (ER), progesterone receptor (PR), HER2neu, and Ki-67 are essential in prognostic and therapeutic stratification of breast carcinoma. While tumor marker evaluation is routine, the adjacent peritumoral region is less studied despite its potential biological significance.

Aim: To evaluate and compare the expression of ER, PR, HER2, and Ki-67 in tumor and peritumoral regions of breast carcinoma and correlate findings with histological grade and lymph node status.

Materials and Methods: This retrospective-prospective study included 43 biopsy-confirmed breast carcinoma cases over a four-year period. Immunohistochemistry was performed for ER, PR, HER2, and Ki-67 on both tumor and peritumoral areas. Molecular classification was done based on IHC profile. Statistical correlation was assessed using appropriate tests.

Results: ER and PR positivity was significantly higher in tumor tissue compared to peritumoral areas. Ki-67 index was also higher in tumor regions. HER2 showed similar expression in both zones. Luminal A was the most frequent molecular subtype, followed by basal-like and HER2-enriched subtypes. A significant association was noted between high Ki-67 index and higher tumor grade and nodal involvement ($p < 0.05$).

Conclusion: Hormonal and proliferative marker expression in peritumoral tissue may offer additional prognostic insight, especially in borderline cases. Integrating peritumoral evaluation with conventional tumor analysis could improve risk stratification and early detection of field changes.

Keywords: *Breast carcinoma, Estrogen receptor, Progesterone receptor, HER 2 neu, Ki-67, Peritumoral lesions, Immunohistochemistry, Molecular subtype*

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1. INTRODUCTION

Breast carcinoma is the most common malignancy and a leading cause of cancer-related mortality among women worldwide. It is a biologically heterogeneous disease with variable clinical behavior, histological patterns, and molecular characteristics. Accurate classification using immunohistochemical (IHC) markers—such as estrogen receptor (ER), progesterone receptor (PR), HER2neu and Ki-67—is essential for guiding therapy and predicting prognosis [1,2].

Although evaluation of these markers in tumor tissue is well established, increasing attention is being paid to the peritumoral region, defined as the adjacent non-neoplastic breast tissue. This region represents a dynamic tumor–host interface that may harbor histological alterations contributing to tumor progression and recurrence [3]. Studies using preoperative MRI have demonstrated that peritumoral edema correlates with aggressive histopathological features such as lymphovascular invasion and stromal fibrosis, underscoring the biological relevance of examining this zone [4].

Ki-67 is a nuclear proliferation marker that strongly correlates with aggressive disease and poor outcomes in breast cancer. Despite its routine use, few studies have directly compared the expression of Ki-67 and hormonal receptors in tumor versus peritumoral tissues. Moreover, imaging-based radiomics features in the peritumoral region—assessed through ultrasound and MRI—have been shown to reflect molecular markers including Ki-67 status [5].

This study aimed to evaluate and compare the IHC expression of ER, PR, HER2 neu and Ki-67 in tumor and peritumoral regions of breast carcinoma, and to correlate these findings with histological grade, lymph node status, and molecular subtype distribution.

2. MATERIALS AND METHODS:

The study was done in 43 cases of Modified Radical Mastectomy and Simple Mastectomy specimens received in the Department of Pathology, Mahatma Gandhi Medical College and Research Institute, Puducherry, for a period of three and half years (December 2021–March 2025) after obtaining approval from the Institutional Human Ethics Committee.

Inclusion Criteria

All Simple mastectomy and Modified Radical Mastectomy specimens with histopathologically proven Invasive carcinoma of the breast. Both sexes were included in the study. Axillary lymph nodes, irrespective of tumor involvement were also studied.

Exclusion Criteria

Tissue blocks with inadequate material and patients treated with neoadjuvant chemotherapy or radiotherapy were excluded. Trucut biopsy or lumpectomy specimens were not included in the study.

Sections taken from the retrieved blocks and tissue obtained from the specimens were used for hematoxylin and eosin (H&E) and immunohistochemistry (IHC) staining. Clinical details, gross morphology, histopathological staging, and tumor grading were retrieved from histopathology request forms and the laboratory information system (LIS). All prospective specimens were received in 10% neutral buffered formalin, fixed for adequate duration, and subsequently processed for H&E and IHC staining.

Tumor Grading and Staging (CAP)

Tumor grading was performed using the Nottingham modification of the Scarff-Bloom-Richardson grading system for invasive breast carcinoma, based on three histological parameters: Tubule formation, Nuclear pleomorphism and Mitotic count. Each parameter was scored from 1 to 3, and the total score was used to classify tumors into Grade I (well-differentiated), Grade II (moderately differentiated), or Grade III (poorly differentiated). Pathological tumor staging was performed according to the AJCC TNM staging system, following the College of American Pathologists (CAP) protocol for Invasive breast carcinoma. Tumor size (pT), regional lymph node involvement (pN), and the presence of distant metastasis (pM, if available) were assessed using histopathological and clinical data.

Immunohistochemistry (IHC)

All cases included in this study underwent IHC evaluation for estrogen receptor (ER), progesterone receptor (PR), HER2neu, and Ki-67. All IHC procedures—including tissue processing, staining, and interpretation—were carried out following the laboratory's standardized operating protocols. Once staining was completed, the slides were independently evaluated by two observers using a binocular compound light microscope at 40× magnification. For IHC, the Streptavidin–biotin–peroxidase complex method was used, with 3-µm thick tissue sections mounted on poly-L-lysine-coated slides.

Scoring for ER and PR

The expression of ER and PR was evaluated using the Allred scoring system, which combines staining intensity (weak, moderate, or strong) and the percentage of tumor cells showing positive nuclear staining (0–100%).

HER2/Neu Scoring (ASCO/CAP)

HER2 expression was evaluated according to the ASCO/CAP scoring system.

Ki-67 Scoring

Ki-67 scoring was determined by the percentage of tumor cells exhibiting nuclear immunostaining, irrespective of intensity. According to the St. Gallen International Consensus of Experts, Ki-67 expression was classified into three groups: low (<10%), intermediate (10–20%), and high (>20%). One high-power field with the highest Ki-67 positivity was selected, and 500 nuclei were counted.

3. RESULTS:

Among the 43 breast carcinoma specimens, Invasive Ductal Carcinoma Not Otherwise Specified (IDC NOS) was the most common diagnosis, comprising 39 cases (90.70%). Invasive Papillary Carcinoma accounted for 2 cases (4.65%). A single case (2.33%) each of Invasive Mucinous Carcinoma (Type B) and Metaplastic Carcinoma infiltrating skeletal muscle at the deep resection margin was also identified.

All patients in the study were female as no male breast cases received during our study period. It was observed that in 25 cases (58.14%), lesions were on the Left side and in 18 cases (41.86%), lesions were on the Right side of the breast. In the present study, MRM was performed for 42 cases (97.6%), whereas for one case (2.33%) simple mastectomy was done.

4. DISTRIBUTION OF CASES ACCORDING TO PERITUMORAL LESIONS

Peritumoral lesions were frequently associated with IDC. IDC with fibrocystic disease was the most common, observed in 30 cases (69.76%). IDC with Ductal Carcinoma In situ (DCIS) and IDC with Adenosis were each seen in five cases (12%). IDC with Usual Ductal Hyperplasia (UDH) was found in two cases (4.65%), and IDC with Atypical Ductal Hyperplasia (ADH) in one case (2.32%).

5. INTRATUMORAL HORMONAL RECEPTOR STATUS

Intratumoral hormonal receptor status showed estrogen receptor (ER) positivity in 25 cases (58.1%), progesterone receptor (PR) positivity in 24 cases (55.8%), and HER2neu positivity in 15 cases (34.9%).

6. PERITUMORAL HORMONAL RECEPTOR EVALUATION

Estrogen (ER) expression was found to be positive in 12 (27.91%) cases in which eight cases of IDC with fibrocystic disease, two cases each in IDC with adenosis and IDC with DCIS. Progesterone expression (PR) was positive in eight cases of IDC with Fibrocystic disease (18.60%). Significantly HER2neu expression in peritumoral lesion was negative in all 43 cases (100%).

7. MOLECULAR CLASSFICATION

Molecular classification based on immunohistochemistry showed Luminal A as the most frequent subtype in 14 cases (32.6%), followed by HER2-enriched in 12 cases (27.9%), Basal-like in 11 cases (25.6%), and Luminal B in six cases (6.98%)—three each in HER2-positive and HER2-negative.

Table 1: Molecular Classification in Relation to Tumor Grade

Molecular Classification	Grade I (n=8)	Grade II (n=16)	Grade III (n=19)	Total (n=43)
Basal-like	3 (37.5%)	2 (12.5%)	6 (33.3%)	11 (25.6%)
HER2-enriched	3 (37.5%)	4 (25%)	5 (27.8%)	12 (27.9%)
Luminal A	1 (12.5%)	7 (43.8%)	6 (31.6%)	14 (32.6%)
Luminal B (HER2-positive)	0	3 (18.75%)	0	3 (7.0%)

Luminal B (HER2-negative)	1 (12.5%)	0	2 (10.5%)	3 (7.0%)
Fisher's exact test applied; p = 0.2467.				

Analysis by tumor grade revealed Grade I tumors most frequently associated with Basal-like and HER2-enriched subtypes (37.5% each). Grade II tumors predominantly showed Luminal A (43.75%), followed by HER2-enriched (25%) and Luminal B (18.75%). Grade III tumors were mainly Luminal A (31.6%), Basal-like (33.3%), and HER2-enriched (27.8%). [Table.1]

Table 2: Molecular Classification in Relation to Nodal Status

Molecular Classification	N0	N1/N1a	N2a	N3	N3a	Total
Basal-like	6 (54.6%)	3 (27.3%)	2 (18.2%)	0	0	11
HER2-enriched	6 (50.0%)	3 (25.0%)	1 (8.3%)	0	2 (16.7%)	12
Luminal A	8 (57.1%)	4 (28.6%)	1 (7.1%)	1 (7.1%)	0	14
Luminal B (HER2-positive)	0	2 (66.7%)	1 (33.3%)	0	0	3
Luminal B (HER2-negative)	1 (33.3%)	1 (33.3%)	1 (33.3%)	0	0	3

Fisher's exact test applied; p = 0.2448.

When correlated with nodal status, Luminal A comprised 14 cases with 57.1% node-negative, and smaller numbers spread across N1, N1a, N2a, and N3 stages. Basal-like included 11 cases, mostly node-negative (54.5%) and N1a (27.3%). HER2-enriched cases (12 total) showed 50% node-negative, with others distributed across N1a, N2a, and N3a. Luminal B HER2-positive cases (three) involved N1a and N2a only, while Luminal B HER2-negative cases (three) were spread across N0, N1a, and N2a. [Table 2]

8. COMPARISON OF HORMONE RECEPTOR EXPRESSION IN BREAST CARCINOMA WITH THEIR CORRESPONDING LYMPH NODE METASTASIS:

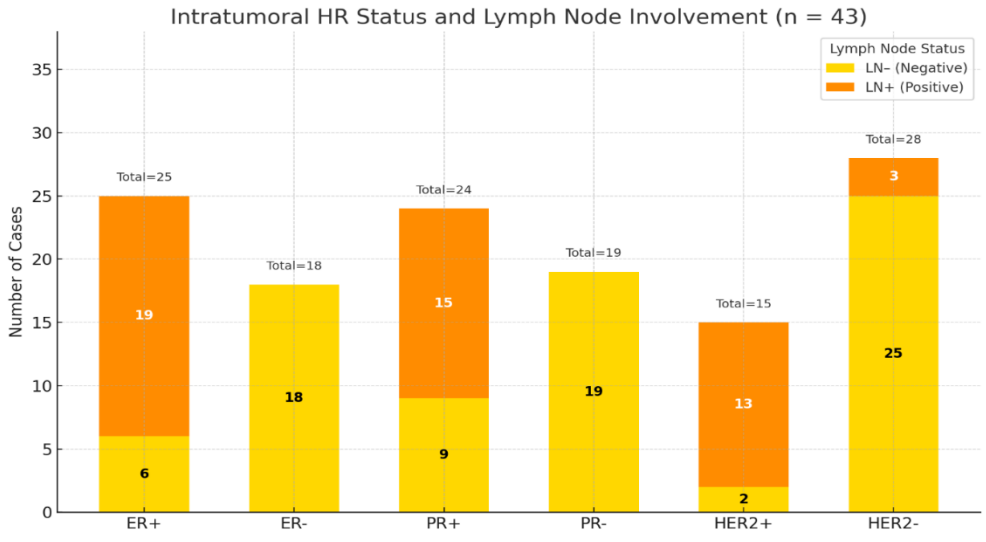

Figure 1: Comparison of ER, PR, and HER2neu Expression in breast carcinoma vs Lymph Node Metastasis

Intratumoral receptor expression in lymph node metastases revealed that of 25 ER-positive cases, 19 showed ER positivity in nodal metastasis, while all ER-negative cases remained negative. For PR, 15 of 24 positive cases retained nodal expression, while all negative cases were negative. Among HER2-positive cases (15 cases), 13 were also positive in nodal metastasis where nine cases showed 3+ staining; three cases showed 2+; one case showed 1 + and two cases showed lymph node negative. In HER2-28 negative cases, 25 remained negative, and three showed nodal positivity. [Figure 1]

9. INTRATUMORAL KI-67 PROTEIN EXPRESSION WITH MOLECULAR SUBTYPES:

Table 3: Intratumoral Ki-67 Expression with Molecular Subtypes

Molecular Subtype	Ki-67 (<10%)	Ki-67 (10–20%)	Ki-67 (>20%)
Luminal A (n=14)	5 (35.7%)	7 (50%)	2 (14.3%)
Luminal B (HER2-positive, n=3)	1 (33.3%)	2 (66.7%)	0
Luminal B (HER2-negative, n=3)	2 (66.7%)	1 (33.3%)	0
HER2-enriched (n=12)	2 (16.7%)	10 (83.3%)	0
Basal-like (n=11)	0	8 (72.7%)	3 (27.3%)
Fisher's exact test applied; p = 0.06.			

Ki-67 expression across molecular subtypes showed that Luminal A included five cases with <10%, seven cases with 10–20%, and two cases with >20%. Luminal B HER2-positive included one case of <10% and two cases with 10–20%. Luminal B HER2-negative had two cases with <10% and one case with 10–20%. HER2-enriched included two cases of <10% and 10 cases with 10–20%. Basal-like showed eight cases with 10–20% and three with >20%. [Table 3]

10. CORRELATION OF INTRATUMORAL KI67 WITH NODAL STATUS:

Table 4: Correlation of Intratumoral Ki-67 with Nodal Status

Nodal Status	Ki-67 (<10%)	Ki-67 (10–20%)	Ki-67 (>20%)
N0 (n=21)	5 (23.8%)	14 (66.7%)	2 (9.5%)
N1 (n=3)	1 (33.3%)	2 (66.7%)	0
N1a (n=10)	3 (30.0%)	7 (70.0%)	0
N2a (n=6)	1 (16.7%)	3 (50.0%)	2 (33.3%)
N3 (n=1)	0	1 (100%)	0
N3a (n=2)	0	1 (50.0%)	1 (50.0%)
Fisher's exact test applied; p = 0.012.			

Among the 43 cases, the N0 group of 21 cases, of which five cases had a Ki-67 index <10%, 14 cases had 10–20%, and two cases showed a higher proliferation index >20%. In the N1 group comprising three cases, one had a Ki-67 index <10% and two had 10–20%. Of the 10 cases in the N1a group, three showed a Ki-67 index <10% and seven had 10–20%. In the N2a group of six cases, one had a Ki-67 index <10%, three had 10–20%, and two demonstrated a higher proliferation index. The single case in the N3 group showed a Ki-67 index of 10–20%, while in the N3a group of two cases, one had Ki-67 values of 10–20% and one exhibited a higher proliferation index.[Table 4]

11. INTRATUMORAL KI-67 INDEX WITH TUMOR GRADE:

Table 5: Comparison of Intratumoral Ki-67 Index with Tumor Grade

Tumor Grade	Ki-67 <10%	Ki-67 10–20%	Ki-67 >20%
Grade I (n=8)	7 (87.5%)	1 (12.5%)	0
Grade II (n=16)	10 (62.5%)	3 (18.8%)	3 (18.8%)
Grade III (n=19)	16 (84.2%)	1 (5.3%)	2 (10.5%)
Chi-square test applied; p = 0.227.			

Grade I tumors were eight cases, of which seven cases showed Ki-67 <10% and one case showed Ki-67 between 10–20%. Grade II comprised 16 cases, with 10 cases had Ki-67 <10% and three cases had 10–20% and three cases in high proliferation index of >20%. Grade III included 19 cases with 16 cases showing Ki-67 <10% and one case with 10–20% expression and high proliferation index >20% in two cases (10.56%). [Table 5]

12. DISTRIBUTION OF PERITUMORAL KI-67 EXPRESSION ACROSS TUMOR GRADES:

Table 6: Peritumoral Ki-67 Expression Across Tumor Grades

Tumor Grade	**Ki-67 <10%**	**Ki-67 10–20%**
Grade I (n=8)	8 (100%)	0
Grade II (n=16)	15 (93.8%)	1 (6.2%)
Grade III (n=19)	16 (84.2%)	3 (15.8%)
Chi-square test applied; p = 0.378.		

Peritumoral Ki-67 expression across tumor grades showed low proliferation (<10%) in 39 cases (91%). This pattern was consistent across Grade I (100%), Grade II (93.8%), and Grade III (84.2%) tumors. Intermediate proliferation (10–20%) was seen in four cases, and high proliferation (>20%) was absent in peritumoral lesions.[Table 6]

13. DISCUSSION:

Our study, which assessed the molecular characteristics of breast carcinoma in a cohort of 43 cases, revealed a distribution of molecular subtypes. The most prevalent subtype in our cohort was Luminal A (32.6%), followed by HER2-enriched (27.9%), Basal-like (25.6%), and two categories of Luminal B (each comprising 7.0% of cases). This pattern shows a relative underrepresentation of the Luminal A subtype, which typically accounts for 50–60% of cases in large multicentre studies, and a notable overrepresentation of the more aggressive HER2-enriched and Basal-like subtypes [6].This shift in proportions is most likely attributed to referral bias within our tertiary care setting, which tends to receive a higher volume of more aggressive, higher-grade tumors, as well as the limited sample size of our study. The proportions for the Luminal B subtypes, however, align closely with published data, underscoring the heterogeneity of this group and its association with more aggressive behaviour and poorer endocrine responsiveness [6,7]

Comparison of Molecular subtype and Histologic Grade:

The correlation between molecular subtypes and tumor grade in our study, while not statistically significant (p = 0.2467), demonstrated trends consistent with the known biology of breast cancer. For instance, Grade III tumors in our cohort were enriched with Basal-like (31.6%) and HER2-enriched (26.3%) subtypes, a finding that is in agreement with reports from other institutional series [8]. This reinforces the established link between high-grade histology and aggressive molecular profiles. However, our data showed an unexpectedly low prevalence of the Luminal A subtype in Grade I tumors (12.5%) compared to other studies that report it to be the most common subtype in well-differentiated lesions. Conversely, we observed a higher-than-expected proportion of Basal-like and HER2-enriched subtypes in our Grade I tumors. These discrepancies are likely influenced by the small sample size and the specific case mix seen in our practice [8,9].

Comparison of Molecular subtype with Lymph node status:

Our analysis of the relationship between molecular subtype and lymph node status further provided insights into the biological behavior of these tumors, even in the absence of a statistically significant association (p = 0.2448). Consistent with literature, Luminal A tumors showed the highest rate of nodal negativity (57.1%).[8] In contrast, HER2-enriched tumors demonstrated a higher propensity for nodal spread, with half of the cases exhibiting nodal metastases, including

advanced involvement, which is comparable to findings in other cohorts.[10] The Basal-like subtype also showed a significant rate of nodal negativity (54.5%), which aligns with the hypothesis that these tumors may favor hematogenous over lymphatic routes for metastasis. Notably, all cases of Luminal B (HER2-positive) in our series exhibited nodal involvement, reinforcing the aggressive nature of this subtype and its potential for higher metastatic burden compared to Luminal A. These differential nodal patterns underscore the importance of molecular subtyping for guiding axillary staging and adjuvant therapy decisions

Our analysis of hormone receptor status demonstrated a strong and significant association between intratumoral receptor expression and lymph node (LN) metastasis. Specifically, 76.0% of ER-positive tumors and 62.5% of PR-positive tumors had LN involvement, whereas no ER-negative or PR-negative cases showed nodal metastasis. These findings are consistent with the literature, as studies by Devadass et al.^8 and Jindal et al [10] similarly reported a higher rate of nodal metastases in hormone receptor-positive tumors, underscoring the role of these receptors as markers of lymphotropic behavior. For HER2neu, 52.0% of HER2-positive tumors were associated with LN metastasis, compared to only 10.7% of HER2-negative cases. This was in concordance with Desouki et al.'s [11] findings and reflects the aggressive and lymphophilic nature of HER2-driven cancers. The strong correlation between positive receptor status and axillary metastasis highlights the critical importance of receptor profiling not only for guiding systemic therapy but also for accurate prognostic stratification and surgical planning.

Comparison of *Intratumoral Ki67 expression with Molecular subtype and Nodal status:*

The Ki-67 proliferation index, a well-established marker of tumor aggressiveness, also showed clear distinctions across our cohort. While the majority of tumors had an intermediate Ki-67 index (10–20%), we observed variations that were consistent with molecular subtypes. Luminal A tumors predominantly had low-to-intermediate Ki-67 levels. Conversely, Basal-like carcinomas, known for their aggressive behavior, showed a high prevalence of intermediate and high proliferation indices, with no tumors falling into the low Ki-proliferation category. More importantly, our study found a statistically significant correlation between a higher intratumoral Ki-67 index and more advanced nodal stages ($p = 0.012$). This observation, particularly the emergence of high Ki-67 expression in $N2_a$ and $N3_a$ tumors, reinforces the clinical utility of Ki-67 as a continuous marker of tumor aggressiveness and metastatic potential. These findings suggest that incorporating Ki-67 into preoperative assessments may be valuable for tailoring the extent of axillary surgery and optimizing adjuvant therapy decisions.

Comparison of Peritumoral lesions with Molecular subtype:

A unique aspect of our study was the evaluation of immunohistochemical markers in the peritumoral region and its correlation with molecular subtypes. We found that fibrocystic change was the most common peritumoral lesion, seen predominantly in Basal-like and Luminal A tumors, a finding that aligns with prior reports by Shushan Jayker et al [12] that linked this peritumoral finding to higher-grade carcinomas. Furthermore, our analysis of other peritumoral lesions largely mirrored findings in the literature. For instance, the association of adenosis with Luminal A tumors supports the hypothesis of a hormonal milieu favoring glandular proliferation in these cases. The occurrence of ductal carcinoma in situ (DCIS) in HER2-enriched and Basal-like tumors, though infrequent, reflects the concept of clonal progression from in situ to invasive disease, as discussed by Rossi et al [13]. Interestingly, we also observed some rare histopathological findings, such as a HER2-enriched invasive papillary carcinoma and a Luminal A Metaplastic carcinoma, which was not statistically generalizable, underscore the biological heterogeneity of breast cancer and its peritumoral interface.

Comparison of Intratumoral Ki-67 expression with Tumor grade:

The correlation between intratumoral Ki-67 expression and histologic grade is a critical component of breast carcinoma subtyping and prognostication. In this study, we observed expected trends in Grade I and II tumors but a surprising finding in Grade III cases. As anticipated, the majority of Grade I carcinomas (87.5%) demonstrated low proliferative activity (Ki-67 <10%), a finding consistent with well-differentiated, low-grade tumors and a favorable prognosis [14]. Grade II tumors, known for their biological heterogeneity, showed a mixed proliferative profile. While a substantial portion (62.5%) had a low Ki-67 index, a significant fraction (nearly 19%) displayed intermediate and high proliferation, reinforcing the role of Ki-67 as a valuable tool for risk stratification within this heterogeneous group [14,15]

Conversely, our findings for Grade III tumors deviated from established literature, where these highly aggressive tumors are typically associated with a high Ki-67 index (>20%). In our cohort, an unexpected 84.2% of Grade III tumors exhibited a low Ki-67 index, with only 10.5% falling into the high proliferation category. This discordance may be attributed to several factors, including potential sampling bias, especially from small core biopsies, or methodological variations in Ki-67 scoring [15]. The importance of standardized assessment protocols, such as global counting versus hot spot methods, has been highlighted in previous studies that demonstrated how scoring techniques can alter the Ki-67 classification of a case [9]. These findings suggest that relying solely on histologic grade may misclassify the proliferative risk in a subset of patients. Therefore, the incorporation of a standardized and reproducible Ki-67 assessment is crucial to refine prognostic stratification and guide therapy, particularly in Grade II and III tumors where an unexpectedly low index may identify candidates for less aggressive treatment.

Comparison of Peritumoral Ki-67 expression with Tumor grade:

Our study also specifically evaluated Ki-67 expression in the peritumoral region, revealing a distinct pattern. In contrast to the variable intratumoral expression, peritumoral tissue consistently exhibited low proliferative activity regardless of the adjacent tumor's grade. This observation aligns with the consensus that Ki-67 is most prognostically informative when measured exclusively within invasive tumor cells, with the peritumoral region typically excluded. This is further supported by studies showing that peritumoral Ki-67 staining is minimal and can confound the overall labeling index. This low peritumoral proliferative activity suggests that the tumor-adjacent microenvironment remains largely quiescent, reflecting reactive changes rather than neoplastic proliferation. From a clinical perspective, these findings reinforce that Ki-67 assessment for adjuvant therapy decisions should focus strictly on the invasive tumor. The quiescence of the peritumoral Ki-67 index may also have implications for understanding tumor–stroma interactions and the development of targeted therapies.This study provides a robust comparative analysis of hormone receptor and Ki-67 expression in both intratumoral and peritumoral regions of breast carcinoma, addressing a notable gap in the existing literature. A key strength is the combined retrospective and prospective design, which enhances the reliability and continuity of the data. The research rigorously applied standardized scoring systems, including the Allred system for ER/PR, ASCO/CAP guidelines for HER2, and the St. Gallen consensus for Ki-67, ensuring objective and reproducible evaluation. The inclusion of molecular subtyping allowed for meaningful correlations between biomarker expression and important prognostic indicators such as tumor grade and lymph node status. Furthermore, the study's finding of high concordance in ER, PR, and HER2 expression between the primary tumor and metastatic lymph nodes adds significant diagnostic value.

14. STRENGTHS AND LIMITATIONS:

This study provides a robust comparative analysis of hormone receptor and Ki-67 expression in both intratumoral and peritumoral regions of breast carcinoma , addressing a notable gap in the existing literature. Despite these strengths, the study is limited by its modest sample size (n = 43) and single-centre design, which may impact the generalizability of the findings and statistical power. Methodological limitations include potential variability in Ki-67 scoring and the lack of fluorescence in situ hybridization (FISH) confirmation for HER2 equivocal cases, which could affect the precision of molecular classification.

15. CONCLUSION:

This study highlights the diagnostic and prognostic relevance of integrating peritumoral marker assessment alongside traditional intratumoral analysis. It revealed significantly lower expression of ER, PR, and Ki-67 in peritumoral regions, reinforcing the biological distinction between tumor and adjacent tissues. Importantly, high Ki-67 index was significantly associated with advanced nodal involvement ($p = 0.012$), affirming its role as a marker of tumor aggressiveness. The high concordance between intratumoral and lymph node receptor status further validates IHC reliability in metastatic settings. While HER2 expression remained confined to tumor cores, its correlation with nodal spread aligns with its aggressive clinical behaviour. Overall, this study advocates for a routine biomarker assessment strategy that includes peritumoral zones to enhance prognostication and treatment planning in breast carcinoma.

Conflict of interest - Nil

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Ethical issues addressed and approved (MGMCRI/RES/01/2022/5/IHEC/74)

The raw data is accessible through the corresponding author and can be reproduced upon legitimate request in accordance with the university's policies

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