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Original Research Article

Correlation of Tumor Grade and Stage with Hormone Receptor Status in Breast Carcinoma: A Study in a Rural Indian Population

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Abstract:

Background: Breast cancer is the most common malignancy among women in India, with rural populations often presenting at advanced stages due to limited healthcare access. Tumor grade, clinical stage, and hormone receptor status (ER, PR, HER2) are critical prognostic and therapeutic indicators.

Aim: To evaluate the correlation between histopathological grade, clinical stage, and hormone receptor status in breast carcinoma patients from a rural Indian population.

Methodology: A retrospective observational study was conducted on 70 female breast cancer patients at Department of Pathology, Darbhanga Medical College and Hospital, Darbhanga, Bihar. Tumor grading was performed using the Nottingham system, clinical staging by AJCC criteria, and hormone receptor status determined by immunohistochemistry. Associations were analyzed using Chi-square tests.

Results: Most tumors were Grade II (54.3%) and Stage II (50%). ER and PR positivity declined with increasing grade and stage: Grade I tumors were ER/PR-positive in 86%/79%, decreasing to 33%/39% in Grade III; Stage I tumors were ER/PR-positive in 80%/70%, dropping to 25% in Stage IV. HER2 positivity increased with grade and stage, highest in Grade III (39%) and Stage III (35%).

Conclusion: Higher tumor grade and advanced stage are associated with hormone receptor negativity and increased HER2 expression. These findings underscore the importance of integrating receptor profiling with clinicopathological evaluation to guide prognosis and personalized therapy in rural populations.

Keywords: Breast carcinoma, Tumor grade, Clinical stage, Hormone receptor, ER, PR, HER2, Rural India.

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Introduction

Breast cancer is the commonest cancer in women globally and a significant issue in the health of the population because it is a highly prevalent, morbid, and fatal cancer. Although there have been tremendous improvements in screening procedures, diagnostic procedures and therapeutic interventions, breast cancer remains the major cause of cancer-related mortality in women all over the world. The burden of the disease is specifically high in developing countries, in which the healthcare infrastructure, deficiency of knowledge and delay in access to diagnostic or treatment resources impose poorer outcomes. The rate of breast cancer in India has been on a continuous rise in the recent decades surpassing cervical cancer as the leading cancer predisposed to women in most parts. Women tend to bring up in the late stages of the disease and as a result of socio-economic reasons, cultural taboos, screening services, and inaccessibility of specialised oncological services, rural populations are being disproportionately affected [1].

Biological behaviour of breast carcinoma is something that must be understood in order to enhance the management of the patients and their survival. Breast cancer is a heterogeneous disease that has a great variation in clinical presentation, histopathological characteristics, molecular characteristics and response to treatment. Histopathological grading and clinical staging are among the key parameters used in prognostication and treatment planning based on established parameters of clinicopathology. The use of histopathological grading shows the extent of tumor differentiation and gives an idea on

the aggressiveness of the malignancy. Grade I (well-differentiated), Grade II (moderately differentiated), and Grade III (poorly differentiated) are characterized by architectural patterns, nuclear pleomorphism, and mitotic activity and come to be classified as a tumour. The general rates of higher grades are correlated with faster development of tumor, the likelihood of metastasis, and unfavourable prognosis.

The Tumour-Node-Metastasis (TNM) system of clinical staging of breast cancer is most often used to determine the size of the original tumour, the involvement of the nearby lymph nodes, and the presence or absence of distant-metastasis. The stage of diagnosis is a one of the most important predictors of survival, and the disease at an early stage has much better prognosis than the disease at an advanced stage. Histopathological grading and clinical staging are used together to complement each other in terms of information about tumour biology, disease severity and anticipated clinical course, hence allowing the therapeutic decision-making process and prognostic analysis [2] to be made.

Besides conventional clinicopathological parameters, the recent technological progress in the field of molecular pathology has demonstrated the important role of hormone receptor status in breast cancer classification and treatment. Breast carcinomas are regularly tested concerning the expression of oestrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). Such receptors do not only act as a prognostic marker but also indicators of response to targeted therapies. The most common types of breast cancer are ER- and PR-positive, which are generally linked to a higher prognosis, reduced histological grade, and increased sensitivity to endocrine treatment. Hormonal therapies of these receptors have also greatly enhanced control and survival of the disease in the affected people.

HER2-positive breast cancers on the other hand are said to be marked by the overexpression or amplification of HER2 oncogene that results in aggressive tumour behaviour and high proliferative activity. These tumours were previously considered to be linked with poor prognosis but the emergence of the HER2-targeted therapies has resulted in a significant betterment of the outcomes. Triple-negative breast cancers, characterized by lack of expression of ER, PR and HER2, represent a unique and especially aggressive form of breast cancer. These tumours tend to be of high grades, are at an advanced stage and do not respond to targeted treatment and thus their treatment is particularly difficult [3].

The association between the status of hormone receptors and diverse clinicopathological characteristics of breast carcinoma has been studied among many studies. It has been indicated that ER-negative and PR-negative tumours are more often related to higher histopathological grades, higher mitotic activity, and higher clinical stages at presentation. Likewise, the aggressive pathological appearances and unfavourable prognostics indicators have been associated with HER 2-positive tumours. These associations demonstrate the significance of the combination of hormone receptor assessments and the conventional grading and staging methodologies in order to have a more qualitative comprehension of tumour conduct and prognosis [4].

Nevertheless, most of the current literature is based on the research that has been carried out in the large urban centres or high-income nations, where access to early detection initiatives, superior diagnostic centres, and contemporary treatment approaches is comparatively prevalent. There is limited information about rural populations and especially in developing nations such as India. There are special problems of rural healthcare settings, such as the slow diagnosis, insufficient pathology, and immunohistochemical tests of hormone receptors. Consequently, there might be different biologic profile and clinicopathological relationships of breast cancer in rural versus urban or resourceful regions.

Considering these gaps in the current knowledge, the evaluation of how histopathological grade, clinical stage, and hormone receptor status are correlated with breast carcinoma cases among people in rural areas of India is urgently needed. These studies can be helpful regarding the patterns of diseases, the ability to investigate high-risk populations, and the creation of picture-specific diagnostic and treatment plans. These correlations might also be understood in order to optimize resource allocation and enhance prognostication and therapeutic outcomes of underserved rural communities.

The current research is expected to determine the relationship between tumour grade and clinical stage and hormone receptor status in individuals with breast carcinoma in a rural Indian set of patients. Through such relations, the study would be able to make its contribution to the available literature and demonstrate the significance of combining clinicopathological and molecular parameters in the overall evaluation of breast cancer, especially in resource-restricted rural areas.

Methodology

Study Design: This was a retrospective observational study conducted to evaluate the correlation between tumor grade, stage, and hormone receptor status in breast carcinoma patients.

Study Area: The study was carried out in the Department of Pathology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India.

Study Duration: The study was conducted over a period from March 2025 to October 2025

Sample Size: A total of 70 female patients diagnosed with breast carcinoma were included in the study.

Inclusion Criteria

- Female patients aged 18 years and above.
- Histopathologically confirmed breast carcinoma.
- Availability of complete medical records, including hormone receptor status (ER, PR, HER2).

Exclusion Criteria

- Patients with recurrent or metastatic breast cancer at initial presentation.
- Incomplete medical records or missing hormone receptor status.
- Patients who received neoadjuvant chemotherapy prior to biopsy.

Sampling Method: Consecutive sampling was employed to minimize selection bias. All eligible patients during the study period were included to ensure representativeness.

Data Collection: Data were collected retrospectively from patient medical records and the hospital cancer registry of Darbhanga Medical College and Hospital. A pre-designed and structured data collection proforma was used to ensure uniformity and accuracy. Information regarding demographic characteristics, including age and sex, histopathological tumor grade, clinical stage at presentation, and hormone receptor status (estrogen receptor [ER], progesterone receptor [PR], and human epidermal growth factor receptor 2 [HER2]) was systematically recorded for each patient. Only cases with complete and verifiable records were included in the analysis.

Procedure: Histopathological evaluation of breast carcinoma specimens was carried out in the Department of Pathology. Tumor grading was performed using the Nottingham histological grading system, which assesses tubule formation, nuclear pleomorphism, and mitotic activity. Clinical staging was assigned according to the American Joint Committee on Cancer (AJCC) staging manual based on tumor size, lymph node involvement, and distant metastasis status. Hormone receptor status was determined by immunohistochemistry (IHC) using standard laboratory protocols. Estrogen receptor, progesterone receptor, and HER2 expression were evaluated following established reporting guidelines, and results were documented in the pathology records.

Statistical Analysis: Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software version 23.0. Descriptive statistics, including frequencies, percentages, means, and standard deviations, were used to summarize demographic data and tumor characteristics. Associations between hormone receptor status and tumor grade as well as clinical stage were analyzed using the Chi-square test. Pearson's correlation coefficient was applied where appropriate to assess the strength of correlation between variables. A p-value of less than 0.05 was considered statistically significant."

Result

Table 1 presents the distribution of histopathological grades and clinical stages among the 70 breast cancer patients studied. With respect to tumor grading, the majority of cases were Grade II, accounting for 54.3% (38/70), followed by Grade III tumors at 25.7% (18/70), while Grade I tumors comprised 20% (14/70) of the study population. Analysis of clinical staging revealed that Stage II disease was most common, observed in 50% (35/70) of patients, followed by Stage III in 24.3% (17/70) and Stage IV in 11.4% (8/70), whereas Stage I tumors constituted 14.3% (10/70) of cases. Overall, Table 1 indicates that most patients presented with moderately differentiated tumors and were diagnosed at intermediate clinical stages, reflecting a tendency toward delayed presentation in the study population.

Table 1: Distribution of Histopathological Grades and Clinical Stages

Characteristic	Number of Patients (n=70)	Percentage (%)
Histopathological Grade		
Grade I	14	20
Grade II	38	54.3
Grade III	18	25.7
Clinical Stage		
Stage I	10	14.3
Stage II	35	50
Stage III	17	24.3
Stage IV	8	11.4

Table 2 summarizes the overall hormone receptor status among the 70 breast cancer patients included in the study. Estrogen receptor (ER) positivity was observed in 60% (42/70) of cases, while 40% (28/70) were ER-negative. Progesterone receptor (PR) expression was evenly distributed, with 50% (35/70) of tumors being PR-positive and an equal proportion 50% (35/70) being PR-negative. HER2

overexpression was identified in 25.7% (18/70) of patients, whereas the majority, 74.3% (52/70), were HER2-negative. Overall, Table 2 indicates that hormone receptor–positive tumors (ER and/or PR) constituted a substantial proportion of cases, while approximately one-quarter of tumors demonstrated HER2 positivity, highlighting the heterogeneity of breast cancer receptor profiles in the study population.

Table 2: Hormone Receptor Status

Hormone Receptor Status	Number of Patients (n=70)	Percentage (%)
ER-positive	42	60
ER-negative	28	40
PR-positive	35	50
PR-negative	35	50
HER2-positive	18	25.7
HER2-negative	52	74.3

Table 3 depicts the association between histopathological grade of breast cancer and hormone receptor status (ER and PR). Well-differentiated tumors (Grade I) showed high hormone receptor expression, with ER positivity in 86% (12/14) and PR positivity in 79% (11/14) of cases. In Grade II tumors, hormone receptor expression declined, with ER positivity observed in 55% (21/38) and PR positivity in 50% (19/38) of patients. Poorly differentiated tumors (Grade III) demonstrated predominantly hormone receptor–negative status, as 67% (12/18) were ER-negative and 61% (11/18) were PR-negative, with ER and PR positivity limited to 33% (6/18) and 39% (7/18), respectively. Overall, Table 3 shows a clear inverse relationship between increasing histopathological grade and hormone receptor expression, indicating that higher-grade tumors are more likely to lack ER and PR expression and exhibit more aggressive biological behavior.

Table 3: Histopathological Grade and Hormone Receptor Status

Histopathological Grade	ER-positive (%)	ER-negative (%)	PR-positive (%)	PR-negative (%)
Grade I (n=14)	86% (n=12)	14% (n=2)	79% (n=11)	21% (n=3)
Grade II (n=38)	55% (n=21)	45% (n=17)	50% (n=19)	50% (n=19)
Grade III (n=18)	33% (n=6)	67% (n=12)	39% (n=7)	61% (n=11)

Table 4 illustrates the relationship between clinical stage of breast cancer and hormone receptor status (ER and PR). Early-stage disease showed higher hormone receptor positivity, with Stage I tumors demonstrating ER positivity in 80% (8/10) and PR positivity in 70% (7/10) of cases. In Stage II, ER and PR positivity declined to 63% (22/35) and 60% (21/35), respectively. A marked shift toward hormone receptor negativity was observed in advanced stages, as Stage III tumors were predominantly ER-negative (65%, 11/17) and PR-negative (59%, 10/17). This trend was more pronounced in Stage IV, where 75% (6/8) of tumors were both ER-negative and PR-negative, with only 25% (2/8) retaining ER or PR positivity. Overall, Table 4 demonstrates a clear inverse association between advancing clinical stage and hormone receptor expression, indicating that advanced-stage breast cancers are more likely to be hormone receptor–negative and biologically aggressive.

Table 4: Clinical Stage and Hormone Receptor Status

Clinical Stage	ER-positive (%)	ER-negative (%)	PR-positive (%)	PR-negative (%)
Stage I (n=10)	80% (n=8)	20% (n=2)	70% (n=7)	30% (n=3)
Stage II (n=35)	63% (n=22)	37% (n=13)	60% (n=21)	40% (n=14)
Stage III (n=17)	35% (n=6)	65% (n=11)	41% (n=7)	59% (n=10)
Stage IV (n=8)	25% (n=2)	75% (n=6)	25% (n=2)	75% (n=6)

Table 5 demonstrates a clear association between HER2 status and both histopathological grade and clinical stage of breast cancer. HER2 positivity increased with worsening tumor grade, being lowest in Grade I tumors at 14% (2/14), rising to 24% (9/38) in Grade II, and highest in Grade III tumors at 39% (7/18), indicating a greater prevalence of HER2-positive disease in poorly differentiated tumors. A similar trend was observed with clinical stage, where HER2 positivity was least in Stage I at 10% (1/10), increased in Stage II to 26% (9/35), and peaked in Stage III at 35% (6/17), followed by 25% (2/8) in Stage IV. Overall, these findings from Table 5 suggest that HER2-positive tumors are more commonly associated with higher histopathological grades and advanced clinical stages, reflecting a more aggressive tumor biology.

Table 5: HER2 Status and Tumor Characteristics		
Tumor Characteristic	**HER2-positive (%)**	**HER2-negative (%)**
Histopathological Grade		
Grade I (n=14)	14% (n=2)	86% (n=12)
Grade II (n=38)	24% (n=9)	76% (n=29)
Grade III (n=18)	39% (n=7)	61% (n=11)
Clinical Stage		
Stage I (n=10)	10% (n=1)	90% (n=9)
Stage II (n=35)	26% (n=9)	74% (n=26)
Stage III (n=17)	35% (n=6)	65% (n=11)
Stage IV (n=8)	25% (n=2)	75% (n=6)

Discussion

The current paper examined the relationship between tumor grade and stage and hormone receptor status in breast carcinoma in a rural Indian setting. Grade II tumors prevailed in our group of 70 patients (54.3) followed by Grade III (25.7) and Grade I (20%). Stage II was the most common (50%), followed by Stage III, I and IV (24.3, 14.3 and 11.4) respectively. The proportion of tumors with estrogen receptor (ER) positivity, progesterone receptor (PR) positivity, and HER2 positivity were 60, 50% and 25.7% respectively. Grade I tumors were found to have the greatest levels of ER and PR (86 and 79 positive, respectively) with Grade III tumors showing significantly lower levels of hormone receptor expression (33% ER-positive and 39% PR-positive) when stratified by histopathological grade. On the same note, the lower the clinical stage, the greater the likelihood of reduced hormone receptor expression, and Stage IV tumors were only 25% ER and PR positive. The HER2 expression exhibited a negative trend as in Grade III (39) and Stage III (35) tumors were more likely to be a HER2-positive tumor. All these findings point to the possibility that higher grade and more advanced stage breast tumors have a more aggressive phenotype that is characterized by hormone receptor negativity and a higher level of HER2."

These results mostly coincide with the previous research studies among Indian populations. The results of Gore et al. (2020) [5] indicated that out of 112 breast cancer patients, 64% of them were ER/PR positive, 13% were ER/PR negative, and Grade III tumors were mostly negative in terms of receptors. They also reported that Stage III tumors constituted the largest percentage of advanced tumors, and this corresponds to our findings of more of the advanced tumors being hormone receptor negative. Similar was observed by Sinam (2019) [6], when a cohort of 180 operable breast cancers were observed, most of the tumors were Grade III (84.5) and a good fraction were ER/PR negative. Higher tumor grade, and hormone receptor negativity as we found can be very much related to these findings as it supports the inverse relationship between the tumor aggressiveness and hormone receptor expression.

Many studies also support the relationship between the HER2 positivity and the tumors with high grades. According to Zodinpuii et al. (2019) [7], the higher the tumor grades were, the greater the level of HER2 positivity and poor prognosis. This is also the case as evidenced in our findings with 39 percent of Grade III tumors being HER2-positive versus 14 percent of Grade I tumors, which highlight the value of HER2 as an indicator of aggressive disease. The negative status of ER, PR, and HER2 in triple-negative tumors (George et al., 2018) [8] was also reported, and this research also indicated that triple-negative tumors are typically Grade III and commonly found in younger and premenopausal women, which also supports the association between hormone receptor negativity, high grade, and tumor aggressiveness.

Compared to clinical staging, the progressive erosion of ER and PR positivity between Stage I and Stage IV in our case is reflective of the same in other Indian cohort studies. As an example, Gore et al. (2020) [5] showed that tumors with high stages had more highly expressed hormone receptor negativity, and the tumor size was linked to more violent phenotypes. Likewise, Sinam (2019) [6] noted that the Stage III tumors were less ER/PR positive underlining the fact that the stage of tumor is an important variable that determines hormone receptor status. This agreement in studies indicates the consistent trend whereby higher-stage tumors of the breast have higher chances of being devoid of hormone receptor expression, which implies late diagnosis or the higher tumor biology in such groups.

There are conflicting observations between PR expressions where in some studies the PR expression was less correlated with tumor grade than the ER. In reference to the ER, Madathiveetil et al. (2021) [9] showed moderate correlation between the cytological and histological grading, however, PR revealed variable correlation, especially in Grade II tumors. PR positivity was lower in Grade I tumors (79% versus 39% Grade I through Grade III) in our study, showing a gradual but steady drop in PR positivity with tumor grade as compared to the occasional results of other studies. These variations can be

population specific or differing in methodological variations in the receptor tests.

In general, the findings of our work and the earlier studies show that the increased histological grade and a high clinical stage in breast carcinoma correlates with low levels of the ER and PR expression and high levels of HER2. This trend detects a more violent tumor phenotype that may have a prognosis and therapeutic impact. The fact that we found similar results with other studies conducted in India is an indicator of the relevance of regular hormone receptor testing, especially in rural areas, to initiate an effective treatment plan. Further, the negative correlation between the status of hormone receptors and the aggressiveness of the tumor underlines the necessity of the early detection programs to enhance the outcome in breast cancer patients.

Conclusion

The research proved that tumor grade, clinical stage and hormone receptor status in breast carcinoma have a definite association among the rural Indians. The positive expression of the estrogen and progesterone receptors was more often observed in low grade and early-stage tumors, whereas the negative expression was more likely in the case of high grade and advanced-stage tumors. The positivity of HER2 was found more in more advanced and higher-grade tumors, but overall, the positivity was lower. These results indicate that differentiation and progression of tumors are highly connected to the presence or absence of hormone receptors, and the receptor profiling of this population is important in prognostication and individualized treatment planning.

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