

Study Of Microvessel Density (MVD), Estrogen Receptor (ER) And Progesterone Receptor (PR) Expression In Correlation With Modified Bloom Richardson (MBR) Grading As Prognostic Indicators In Breast Carcinoma

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ABSTRACT

Introduction: Globally, breast cancer is the most prevalent cancer to be diagnosed in women. In India, it makes around 5–8% of all cancer cases. Numerous pathological and clinical prognostic indicators are important in the treatment of breast cancer.

Aim: To study Microvessel density (MVD), Estrogen receptor (ER) and Progesterone receptor (PR) in correlation with Modified Bloom Richardson grading as prognostic indicators in breast carcinoma.

Materials & Methods: The study was designed as a cross-sectional observational study and was conducted in the Department of Pathology at Gandhi Hospital Secunderabad. The study duration was from October 2022 to March 2024, and a total of 40 patients were included as the sample size.

Result: In our study ER expression showed no significant association with the number of lymph nodes involved, with 17 ER-positive (59%) and 7 ER-negative (64%) cases in the node-negative group, and similar distributions across 1–3, 4–9, and ≥10 nodes ($p = 0.7$). In contrast, lymphovascular invasion (LVI) was significantly associated with ER status. Among 13 cases with LVI, 5 were ER-positive (18%) and 8 ER-negative (72%), while in 27 cases without LVI, 24 were ER-positive (82%) and 3 ER-negative (28%) ($p = 0.0008$).

Conclusion: We found that the majority of the 40 patients with breast cancer were between the ages of 41 and 50. While Grade 1 tumors frequently had low microvessel density (MVD), Grade 2 and Grade 3 tumors tended to have high MVD.

Keywords: MVD, Prognostic indicators, Tumor grade, Angiogenesis and Breast carcinoma

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1. INTRODUCTION

Globally, breast cancer is the most prevalent cancer to be diagnosed in women [1]. In India, it makes for 5–8% of all cancers [2]. Numerous pathological and clinical prognostic indicators are important in the treatment of breast cancer [3]. Finding trustworthy prognostic markers is essential to directing clinical management and enhancing patient outcomes since, despite major improvements in treatment modalities, the prognosis of breast cancer still varies greatly. Estrogen receptor (ER) and progesterone receptor (PR) expression, as well as Angiogenesis, have become important factors in determining the behavior of breast cancer and its response to treatment [4,5]. The likelihood of a response to hormonal therapy, which aids in prognostication, increases with the expression of ER and PR in breast cancer [6]. Tumor growth and metastasis are

significantly influenced by hormone receptor status as well as tumor angiogenesis, which is defined by the development of new blood vessels. Tumor vascularity is measured by microvessel density (MVD), which is a surrogate marker for angiogenesis and has been linked to the aggressiveness and progression of breast cancer. Tumor prognosis can be better understood by using histological grading systems like the Modified Bloom Richardson (MBR) grading system. MBR grading divides breast cancers into discrete prognostic groups by evaluating tubule development, nuclear morphology, and mitotic activity, which helps with treatment selection. The expression of three such prognostic indicators—microvessel density, ER, and PR status—in breast cancer has thus been assessed in the current study, along with their associations with other prognostic indicators such as lymphnode involvement, lymphovascular invasion, and the Modified Bloom Richardson grading system.

2. MATERIALS AND METHODS

Type of Study: A crosssectional observational study

Place of Study: Department of Pathology, Gandhi Hospital Secunderabad

Study Duration: October 2022 to March 2024

Sample Size: 40 patients

Inclusion Criteria:

- Mastectomy specimens in female patients diagnosed with breast carcinoma were included.
- All variants of invasive Ductal cell carcinoma were included.
- Patients of all age groups were included

Exclusion Criteria:

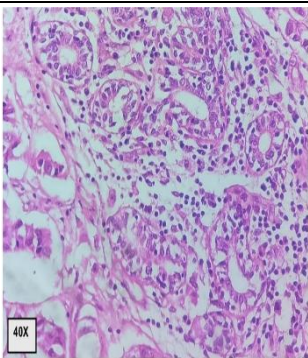
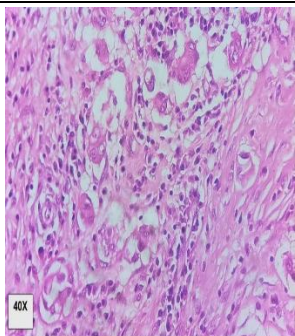
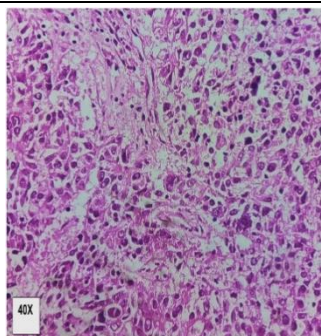
- Poorly preserved specimens with artifacts.
- Patients with unobtainable data are excluded.
- Patients with concurrent other malignant tumors and on treatment for the same are excluded

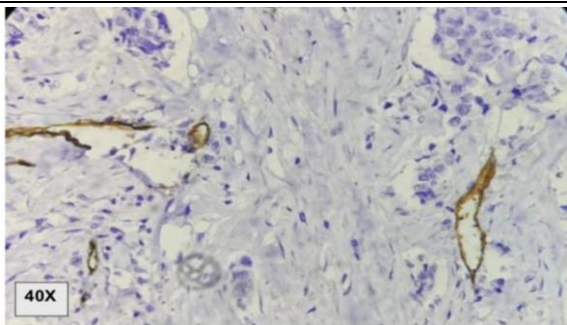
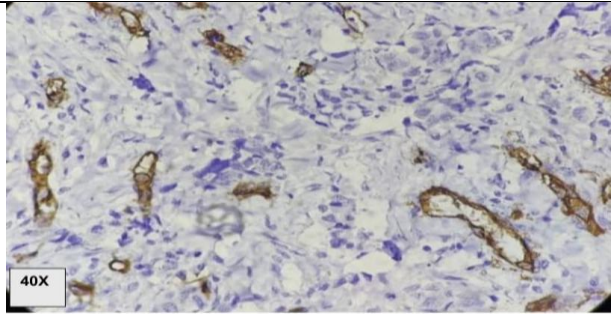
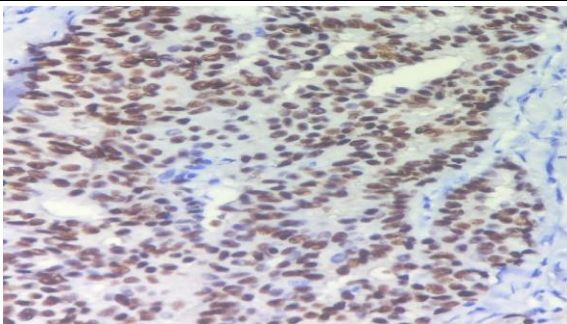
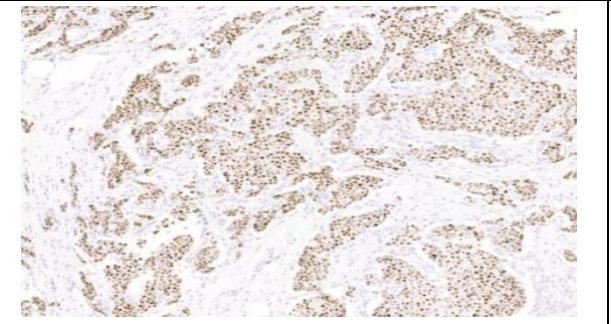
Study Variables:

- Patient age
- Tumour size
- Histological subtype of breast carcinoma
- Correlation of MVD with tumour grade
- Micro vessel Density (MVD) measured using CD34 marker

Statistical Analysis:

Data Were Entered Into Excel And Analyzed Using SPSS And GraphpadPrism. Numerical Variables Were Summarized Using Means And Standard Deviations, While Categorical Variables Were Described With Counts And Percentages. Two-Sample T-Tests Were Used To Compare Independent Groups, While Paired T-Tests Accounted For Correlations In Paired Data. Chi-Square Tests (Including Fisher's Exact Test For Small Sample Sizes) Were Used For Categorical Data Comparisons. P-Values ≤ 0.05 Were Considered Statistically Significant.

		
High power (40X) image of invasive Duct cell carcinoma grade 1 (H&E)	High power (40X) image of invasive Duct cell carcinoma grade 2 (H&E)	High power (40X) image of invasive Duct cell carcinoma grade 3 (H&E)

	
High power (40X) IHC (CD34) image of invasive duct cell carcinoma showing low microvessel Density (MVD)	High power (40X) IHC (CD34) image of invasive duct cell carcinoma showing high microvessel Density (MVD)
	
High power (40X) IHC image ofInvasive duct cell carcinoma showing ER positivity	High power (40X) IHC image ofInvasive duct cell carcinoma showing PR positivity

3. RESULT

Table1: Age Distribution of cases

Age of the patient	Number of cases	Percentage	P- Value
30-40 years	12	30%	0.02202
41-50 years	14	35%	
51-60 years	9	23%	
61-70 years	5	12%	
Total	40	100%	

Table 2:Histological grade of the tumor, ER and PR expression, lymph node involvement, and micro vessel density (MVD)

		LOW MVD	HIGH MVD	P- VALUE
HISTOLOGICAL GRADE	Grade 1 (14)Score (3-5)	12 (85%)	02 (15%)	0.0002
	Grade 2 (20)Score (6-7)	04 (20%)	16 (80%)	
	Grade 3 (6)Score (8-9)	01 (16%)	05 (84%)	
	Total (40)	17	23	
ER EXPRESSION	Positive (29)	16 (94%)	13 (56%)	0.008
	Negative (11)	01 (6%)	10 (44%)	

	Total Cases (40)	17 (100%)	23 (100%)	
PR EXPRESSION	Positive (24)	14 (82%)	10 (43%)	0.013
	Negative (16)	03 (18%)	13 (47%)	
	Total cases (40)	17 (100%)	23 (100%)	
Number of lymphnodes involved	0 Lymphnodes (24)	11 (45%)	13 (55%)	0.59
	1-3 Lymphnodes (11)	03 (27%)	08 (73%)	
	4-9 Lymphnodes (3)	02 (67%)	01 (33%)	
	>= 10 Lymphnodes (2)	01 (50%)	01 (50%)	
	Total cases (40)	17	23	

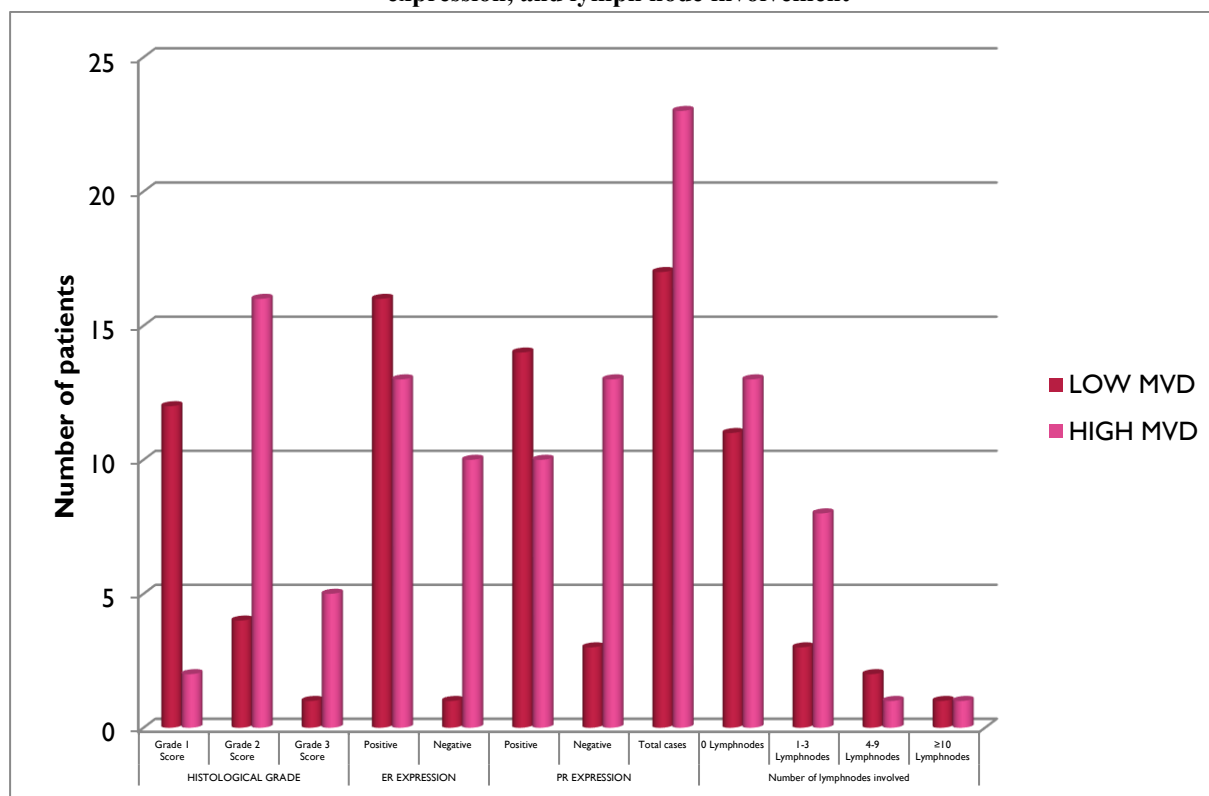
Table3:Association of estrogen receptor (ER) expression with lymph node involvement and lymphovascular invasion (LVI)

		ER positive	ER negative	P value
Number of lymphnodes involved	0 Lymphnodes (24)	17 (59%)	7 (64%)	0.7
	1-3 Lymphnodes (11)	9 (31%)	2 (18%)	
	4-9 Lymphnodes (3)	2 (7%)	1 (8%)	
	≥10 Lymphnodes (2)	1 (3%)	1 (8%)	
	Total cases (40)	29 (100%)	11 (100%)	
LVI	Present (13)	05 (18%)	8 (72%)	0.0008
	Absent (27)	24 (82%)	03 (28%)	
	Total cases (40)	29	11	

Table4:PRExpressioninAssociationwith LN Involvement and LVI:PR

		PR positive	PR negative	P value
Number of lymphnodes involved	0 Lymphnodes (24)	14 (58%)	10 (62%)	0.9
	1-3 Lymphnodes (11)	07 (30%)	04 (26%)	
	4-9 Lymphnodes (3)	02 (8%)	01 (6%)	
	≥10 Lymphnodes (2)	01 (4%)	01 (6%)	
	Total cases (40)	24 (100%)	16 (100%)	
Lymphovascular invasion	Present (13)	03 (13%)	10 (62%)	0.0009
	Absent (27)	21 (87%)	06 (38%)	
	Total cases (40)	24	16	

Figure 1: Assessment of tumor histological grade, estrogen receptor (ER) and progesterone receptor (PR) expression, and lymph node involvement



In our study, out of a total of 40 patients, most were in the 41–50 years age group with 14 patients (35%), followed by 30–40 years with 12 patients (30%), 51–60 years with 9 patients (23%), and 61–70 years with 5 patients (12%). The age distribution among the patients was statistically significant ($p = 0.022$). In our study, microvessel density (MVD) showed significant associations with histological grade and hormone receptor status, while no significant correlation was observed with lymph node involvement. Analysis by histological grade revealed that low MVD predominated in Grade 1 tumors, with 12 of 14 cases (85%) exhibiting low MVD, whereas high MVD was more common in Grade 2 (16/20, 80%) and Grade 3 tumors (5/6, 84%) ($p = 0.0002$), indicating increased angiogenesis with higher tumor grade. Regarding estrogen receptor (ER) expression, 16 of 29 ER-positive tumors (94%) had low MVD, while high MVD was observed in 10 of 11 ER-negative cases (44%), demonstrating a significant inverse association ($p = 0.008$). Similarly, progesterone receptor (PR) expression was associated with MVD, with low MVD seen in 14 of 24 PR-positive tumors (82%) and high MVD more frequent in PR-negative tumors (13/16, 47%) ($p = 0.013$). In contrast, lymph node involvement did not show a statistically significant correlation with MVD ($p = 0.59$), with variable distribution across groups with 0, 1–3, 4–9, and ≥ 10 involved nodes. ER expression showed no significant association with the number of lymph nodes involved, with 17ER-positive (59%) and 7ER-negative (64%) cases in the node-negative group, and similar distributions across 1–3, 4–9, and ≥ 10 nodes ($p = 0.7$). In contrast, lymphovascular invasion (LVI) was significantly associated with ER status. Among 13 cases with LVI, 5 were ER-positive (18%) and 8 ER-negative (72%), while in 27 cases without LVI, 24 were ER-positive (82%) and 3 ER-negative (28%) ($p = 0.0008$). In our study, low MVD was predominant in Grade 1 tumors (12, 85%), while high MVD was more frequent in Grade 2 (16, 80%) and Grade 3 tumors (5, 84%) ($p = 0.0002$). Low MVD was mostly seen in ER-positive (16, 94%) and PR-positive tumors (14, 82%), whereas high MVD was common in ER-negative (10, 44%) and PR-negative cases (13, 47%) ($p = 0.008$ and 0.013 , respectively). ER and PR expression showed no significant association with the number of lymph nodes involved, with most node-negative cases being ER-positive (17, 59%) and PR-positive (14, 58%) ($p = 0.7$ and 0.9). However, both ER-negative (8, 72%) and PR-negative (10, 62%) tumors were significantly associated with the presence of lymphovascular invasion ($p = 0.0008$ and 0.0009).

4. DISCUSSION

In our study, out of 40 patients most of the patients were 41–50 years old [14 (35.0%)] which was statistically significant ($p=0.02202$). In similar study by Bharat Jindal et al [7] with mean patient age of 48 years. and V.Vijayasree et al [8] with mean patient age of 49 years.

We found that, high MVD was most frequent in Grade 2 (16 patients, 80%) and Grade 3 tumors (5 patients, 84%), while low MVD predominated in Grade 1 (12 patients, 85%) ($p = 0.0002$). Regarding hormone receptor status, low MVD was

greater in ER-positive cases (16 patients, 94%) and PR-positive cases (14 patients, 82%), whereas high MVD was more common in ER-negative (10 patients, 44%) and PR-negative tumours (13 patients, 47%) ($p = 0.008$ and 0.013 , respectively). In terms of lymph node involvement, high MVD was most frequent in patients with 1–3 nodes involved (8 patients, 73%), although the association was not statistically significant ($p = 0.59$). In other study by **Agnani [9] et al. (2020)** titled "Prognostic significance of microvessel density as assessed by anti-CD34 monoclonal antibody in invasive ductal carcinoma of the breast closely aligns with our findings.

We observed that, ER expression showed no significant association with the number of lymph nodes involved. Among node-negative cases, 17 patients (59%) were ER-positive and 7 patients (64%) were ER-negative. In patients with 1–3 nodes involved, 9 (31%) were ER-positive and 2 (18%) ER-negative; in the 4–9 node group, 2 (7%) were ER-positive and 1 (8%) ER-negative; while in ≥ 10 node cases, 1 patient (3%) was ER-positive and 1 (8%) ER-negative ($p = 0.7$). In contrast, lymph vascular invasion (LVI) was significantly associated with ER status. Among 13 cases with LVI, 8 (72%) were ER-negative and 5 (18%) ER-positive, whereas in 27 cases without LVI, 24 (82%) were ER-positive and 3 (28%) ER-negative ($p = 0.0008$). In other study by **Çavdar et al. [10] (2022)** titled "Predictors of lymphovascular invasion in estrogen receptor-positive breast cancer patients treated with neoadjuvant chemotherapy" aligns closely with our findings.

We showed that, PR expression did not show a significant association with the number of lymph nodes involved. Among node-negative cases, 14 patients (58%) were PR-positive and 10 (62%) were PR-negative. In patients with 1–3 nodes involved, 7 (30%) were PR-positive and 4 (26%) PR-negative; in the 4–9 node group, 2 (8%) were PR-positive and 1 (6%) PR-negative; while in ≥ 10 node cases, 1 patient (4%) was PR-positive and 1 (6%) PR-negative ($p = 0.9$). In contrast, lymphovascular invasion (LVI) was significantly associated with PR status. Among 13 cases with LVI, 10 (62%) were PR-negative and 3 (13%) PR-positive, whereas in 27 cases without LVI, 21 (87%) were PR-positive and 6 (38%) PR-negative ($p = 0.0009$). In similar study by **Erdoğan et al. [11] (2025)** titled "Role of Progesterone Receptor Level in Predicting Axillary Lymph Node Metastasis in Early-Stage Breast Cancer" aligns with our findings regarding the association between progesterone receptor (PR) expression and lymph node involvement.

5. CONCLUSION

We concluded that the majority of the 40 patients with breast cancer were between the ages of 41 and 50. While Grade 1 tumors frequently had low microvessel density (MVD), Grade 2 and Grade 3 tumors tended to have high MVD. While high MVD was linked to ER-negative and PR-negative tumors, low MVD was more common in ER-positive and PR-positive patients. ER and PR expression were highly correlated with lymphovascular invasion but did not significantly correlate with lymph node involvement. These results suggest that MVD, which reflects tumor aggressiveness and metastatic potential, can be a significant prognostic factor in breast cancer, in conjunction with ER and PR status.

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