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Original Research Article

Advancing Breast Cancer Prognostics: The Pivotal Role of MUC1 Biomarker in Global and Indian Contexts

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Abstract:

Background: Breast carcinoma remains a leading cause of cancer-related mortality among women globally, necessitating improved biomarkers for prognosis and treatment stratification. MUC1, a transmembrane glycoprotein, has been implicated in various cancers but its prognostic value in breast cancer remains underexplored in Indian populations.

Objective: To evaluate the association of MUC1 expression with clinico-pathological parameters including tumor grade, hormone receptor status, and lymphovascular invasion in patients with breast carcinoma.

Methods: This retrospective study analyzed 100 slides of confirmed cases of breast carcinoma at Maharshi Devraha Baba Autonomous Medical College, Deoria, UP, from November 2022 to October 2023. MUC1 expression was assessed via immunohistochemistry and correlated with tumor grade, estrogen receptor (ER), progesterone receptor (PR), HER2 status, and presence of lymphovascular invasion using chi-square tests for categorical data.

Results: MUC1 was positively expressed in 73% of the cases. Significant associations were found between MUC1 positivity and higher tumor grades ($p = 0.002$), Luminal B subtype triple negative, and HER 2 enriched carcinomas. The presence of lymphovascular invasion ($p = 0.01$). MUC1 expression was notably higher in more aggressive tumor subtypes, suggesting its potential role in identifying patients with poorer prognosis.

Conclusion: The study underscores the significance of MUC1 as a prognostic marker in breast carcinoma, correlating with more aggressive disease features. MUC1 could serve as a valuable biomarker for refining prognosis and tailoring treatment strategies in breast cancer management. Further studies are recommended to validate these findings and explore the mechanistic roles of MUC1 in breast cancer progression.

Keywords: MUC1, breast carcinoma, prognostic marker, hormone receptors, lymphovascular invasion

Introduction

Breast cancer remains one of the most formidable challenges in oncology, representing the most common cancer among women worldwide [1]. Despite significant advancements in detection and treatment, the variability in prognosis and outcomes persists, underscoring the urgent need for more precise biomarkers that can guide therapy and predict disease progression [2]. Among these potential biomarkers, Mucin 1 (MUC1), a transmembrane glycoprotein expressed on the apical surface of epithelial cells, has garnered attention for its role in tumorigenesis and potential as a prognostic marker [3].

Globally, studies have indicated that MUC1 is not only overexpressed in a substantial proportion of breast cancer cases but is also involved in crucial signaling pathways that promote cancer cell survival and metastasis [4,5]. This has led to its consideration as a target for immunotherapy and as a critical factor in cancer prognosis. In India, where breast cancer incidence has seen a worrying increase due to urbanization and lifestyle changes, the exploration of MUC1 provides a promising avenue to enhance clinical outcomes and personalize breast cancer management [6].

This article seeks to bridge the global research findings with the Indian clinical context, highlighting how MUC1's role as a prognostic marker could be pivotal in the region's fight against breast cancer. By comparing international data with local studies, it aims to present a comprehensive view of MUC1's implications in global and Indian

settings, underscoring the need for targeted research and tailored therapeutic strategies. As breast cancer's burden grows, understanding and leveraging biomarkers like MUC1 could be key to improving survival rates and quality of life for patients across diverse populations.

Methodology

Study Design: The study was designed as a retrospectuive analysis to evaluate the prognostic significance of the MUC1 immunohistochemical marker in breast carcinoma. It aimed to correlate the expression of MUC1 with clinicopathological parameters, tumor characteristics, and hormone receptor statuses (molecular classification) and lymphovascular invasion.

Study Setting: The research was conducted in the Pathology Department at Maharshi Devraha Baba Autonomous Medical College, Deoria, Uttar Pradesh. The study period spanned from 1st November 2022 to 31st October 2023.

Participants: The study included all diagnosed cases of breast carcinoma in Uttar Pradesh at different college. A total of 100 cases slides were analyzed, ensuring they met inclusion criteria such as comprehensive clinical and pathological details (age, gender, histological diagnosis, tumor grade, lymphovascular invasion, etc.).

Bias: To reduce selection bias, the study included consecutive cases of breast carcinoma during the study period. Information bias was minimized by using a standardized proforma for data collection and adhering to consistent methods in histopathological processing and reporting.

Variables: The primary variable of interest was the expression of MUC1, determined through immunohistochemical staining and categorized as positive or negative. Secondary variables included demographic data (age, gender), tumor histological type and grade, hormone receptor status (ER, PR, HER2/neu and Ki67), and other clinical outcomes like lymphovascular invasion.

Data Collection: Data were systematically collected using a prevalidated proforma that captured details from each case, including demographics, clinical history, histopathological diagnosis, and results from immunohistochemical staining for MUC1, ER, PR, HER2/neu, and Ki67.

Procedure: Tissue specimens were fixed in formalin, embedded in paraffin, sectioned, and stained using hematoxylin and eosin. This was followed by immunohistochemical staining for the study markers. The staining process and evaluation were performed according to standardized protocols to maintain consistency across all samples.

Statistical Analysis: Data were entered into SPSS software (version 23.0) for analysis. Descriptive statistics were used to summarize the characteristics of the study population. The association between MUC1 expression and various clinicopathological features was assessed using the chi-square test. A p-value of ≤ 0.05 was adopted as the threshold for statistical significance.

Results

Participant Demographics and Clinical Characteristics: The study analyzed 100 cases of breast carcinoma with a majority of the patients being female (98%). The age of participants ranged from 31 to 65 years, with a mean age of 47 years. Histologically, the most common type of breast cancer observed was invasive ductal carcinoma (75%), followed by lobular carcinoma (15%) and other types (10%)

MUC1 Expression: MUC1 positivity was detected in 73% of the cases.

Association with Clinico-pathological Features and Hormone receptors: The analysis revealed significant associations between MUC1 expression and several clinicopathological parameters:

- Tumor Grade: MUC1 expression was significantly associated with higher tumor grades. About 100% of grade III tumors exhibited MUC1 positivity compared to only 40% in grade I tumors ($p = 0.002$).

- Hormone Receptor Status: MUC1 positivity was more prevalent in Luminal B tumors which are ER positive, PR low positive and variable HER 2 expressions with intermediate or high prolyeration rate (Ki-67), HER 2 enriched and triple negative carcinomas

- Lymphovascular Invasion (LVI): A significant association was observed between MUC1 expression and the presence of LVI, with 70% of MUC1 positive cases showing LVI ($p = 0.01$).

Statistical Analysis: Chi-square tests confirmed the significance of the relationships between MUC1 expression and tumor grade, hormone receptor status, and LVI, with p-values less than 0.05. The strength of association was further quantified using odds ratios, indicating that MUC1 positive tumors were twice as likely to be high-grade compared to MUC1 negative tumors.

Table 1: Demographic and Clinical Characteristics of Study Participants

Characteristic	Total Number (N=100)	MUC1 Positive (n=73)	MUC1 Negative (n=27)	p-value
Age Range	31-65	-	-	
Mean Age	47	-	-	
Gender				
Female	98	72	26	
Male	2	1	1	
Histological Type				
Invasive Ductal	75	55	20	
Lobular	15	11	4	
Other Types	10	7	3	

Table 2: Association of MUC1 Expression with Tumor Grade

Tumor Grade	MUC1 Positive (n=73)	MUC1 Negative (n=27)	MUC 1 Positive %	p-value
Grade I	10	15	40%	0.002
Grade II	30	12	71%	
Grade III	33	0	100%	

Table 3: Association of MUC1 Expression with Lymphovascular Invasion

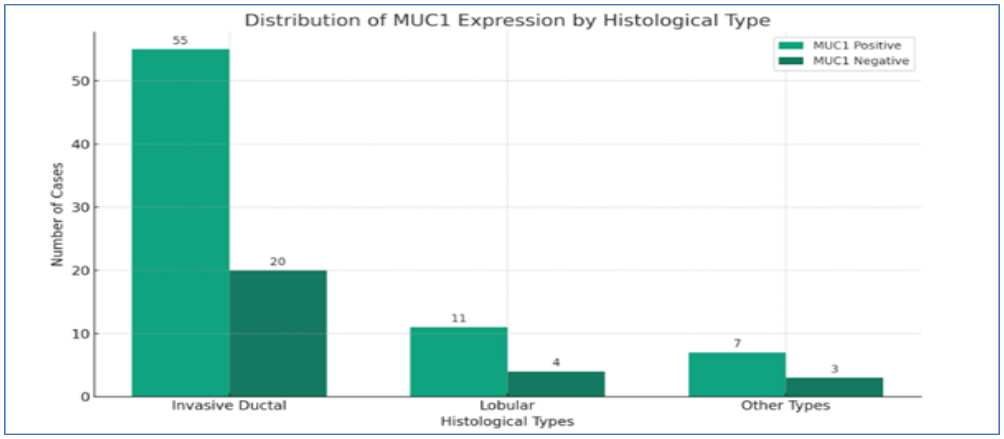
LVI Status	MUC1 Positive (n=73)	MUC1 Negative (n=27)	p-value
Present	51	11	0.01
Absent	22	16	

Table 4: Association of Molecular classification with MUC-1 of study subjects

		MUC 1		Total	P value
		Negative	Positive		
Molecular Classification	HER 2 ENRICHED	2	15	17	0.1
	Luminal A Subtype	5	11	16	0.75
	Luminal B	18	27	45	0.01
	Triple Negative	3	19	22	0.089
Total		28	72	100	

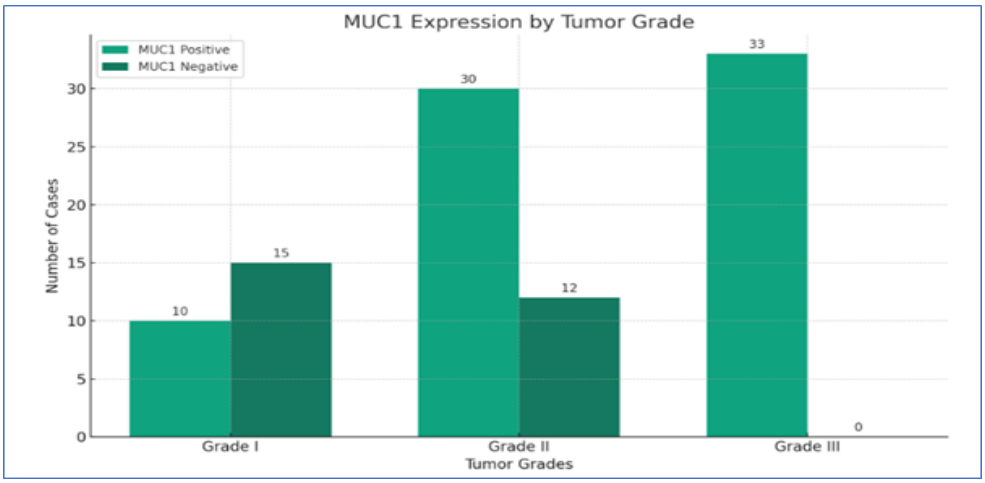
		MUC 1		Total	P Value
		Negative	Positive		
Luminal B	HER 2 +	12	12	24	
	HER 2 -	6	15	21	0.143

Table 4 shows the association of Molecular classification with MUC-1 of study subjects, Majority of study subjects (45%) were Luminal B subtype, in which 27 subjects were MUC-1 positive, whereas 18 subjects were MUC-1 negative. out of 22 triple negative study subjects 19 subjects were MUC-1 positive and 3 subjects were MUC-1 negative. 16 subjects were luminal A subtype in which 11 were MUC-1 positive and 5 subjects were negative, on applying Z test for the proportion of two groups, it was insignificant for all the molecular types except the Luminal B subtype, for which the p-value was 0.01.No association was found between MUC1 and luminal B HER-2 Negative and luminal B HER-2 Positive with p value of 0.143.



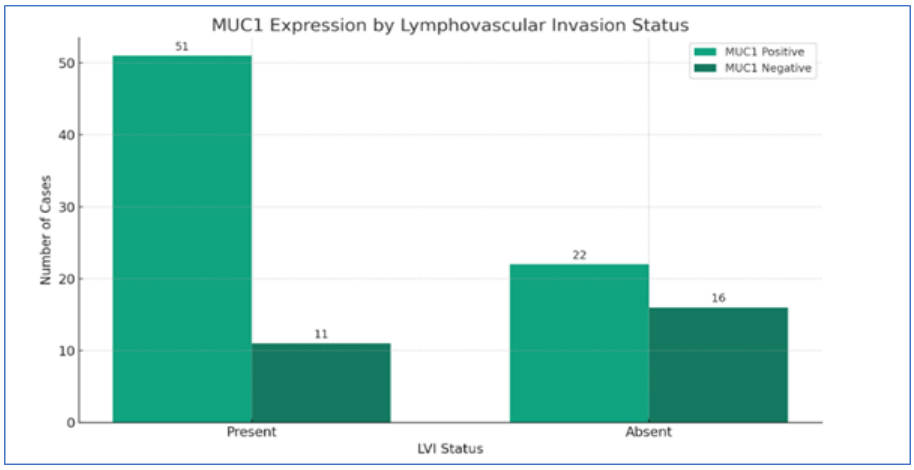
1. Distribution of MUC1 Expression by Histological Type:

This graph displays the number of MUC1 positive and negative cases across different histological types (Invasive Ductal, Lobular, and Other Types).



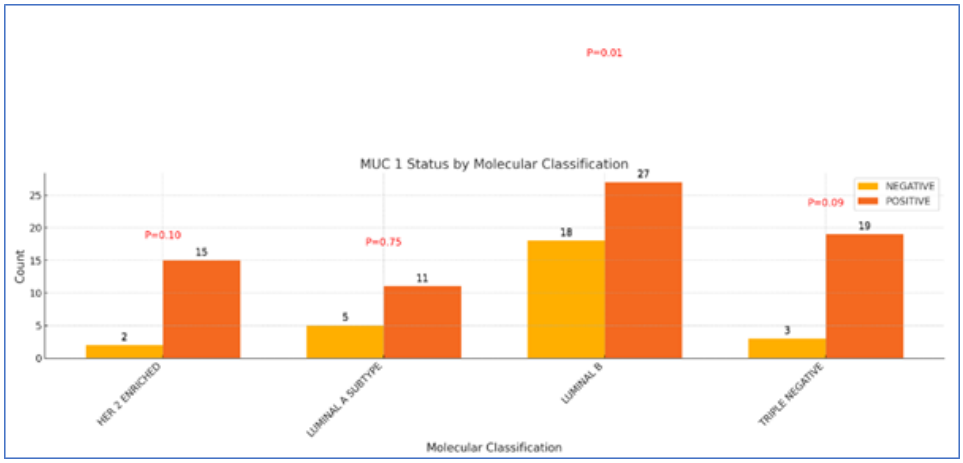
2. MUC1 Expression by Tumor Grade:

This graph illustrates the distribution of MUC1 expression across different tumor grades (Grades I, II, III), showing a higher expression in higher grades.



3. MUC1 Expression by Lymphovascular Invasion (LVI) Status:

This graph shows the correlation between MUC1 expression and the presence of lymphovascular invasion, with a higher incidence of MUC1 positivity in cases where LVI is present.



4. MUC1 status by Molecular Classification

Discussion

The slide studied at Maharshi Devraha Baba Autonomous Medical College, Deoria, investigated the expression of MUC1 in breast carcinoma and its correlation with various clinico-pathological parameters. The findings indicate that MUC1 is predominantly expressed in more aggressive and advanced forms of breast cancer, particularly in tumors that are higher grade and luminal B, HER 2 enriched and triple negative carcinoams [6,7].

The significant association between MUC1 expression and higher tumor grades (II and III) aligns with previous research suggesting that MUC1 plays a role in tumor progression and malignancy [8]. MUC1 is known for its involvement in cell adhesion, signaling, and immune recognition, which can influence tumor growth and metastasis. The higher expression in more aggressive tumors underscores its potential role as a marker for poor prognosis and as a therapeutic target [9].

The study found a strong correlation between MUC1 positivity and hormone receptor status, particularly with luminal B[10]. This result is consistent with existing literature indicating that MUC1 interacts with hormone receptor signaling pathways, potentially influencing the responsiveness of tumors to hormone therapies. The association with HER2-positive status further suggests that MUC1 could be integral in the complex network of pathways that drive aggressive breast cancer phenotypes [11].

The presence of lymphovascular invasion (LVI) was significantly associated with MUC1 positivity, highlighting its potential role in cancer invasiveness and metastatic potential. Since LVI is a critical factor in the spread of cancer cells through the circulatory system, MUC1's association with LVI could help in identifying patients at higher risk of metastasis, thereby guiding more aggressive treatments [12].

The findings of this study have several implications for the management of breast cancer. The strong correlation between MUC1 expression and factors associated with poor prognosis could aid in the stratification of patients based on their risk, potentially leading to tailored treatment approaches [13]. Additionally, the role of MUC1 in various signaling pathways makes it a viable target for novel therapeutic strategies, including vaccines and antibody therapies that could disrupt its function in tumor cells [14].

Comparing these results with global studies, the expression patterns and associations of MUC1 in this Indian cohort are similar to those reported in other populations [15]. This consistency supports the generalizability of MUC1 as a prognostic marker across diverse demographic backgrounds. However, studies in different regions might reveal unique interactions between genetic backgrounds and environmental factors influencing MUC1 expression [16].

While the study provides valuable insights, it has limitations, including its cross-sectional design, which precludes establishing causality between MUC1 expression and clinical outcomes [17]. Longitudinal studies are needed to better understand the temporal relationship between MUC1 expression and breast cancer progression. Additionally, the study could benefit from a larger sample size to enhance the statistical power and enable more detailed subgroup analyses [18].

Future research should focus on longitudinal studies to track changes in MUC1 expression over time and its direct impact on treatment outcomes. Furthermore, exploring the molecular mechanisms underlying MUC1's role in breast cancer could unveil more targeted interventions. Integrating genetic and environmental factors could also provide deeper insights into the variability in MUC1 expression and its clinical implications [18,19,20].

Conclusion

This study at Maharshi Devraha Baba Autonomous Medical College, Deoria, establishes MUC1 as a significant prognostic marker in breast carcinoma, associated with higher tumor grades, positive hormone receptor status, and lymphovascular invasion. These findings suggest that MUC1 expression can identify patients with more aggressive and potentially poorer prognostic breast cancers, highlighting its role in guiding more targeted and intensive treatment strategies. Given the correlation between MUC1 positivity and advanced disease features, integrating MUC1 testing into routine clinical diagnostics could enhance patient stratification and management. Future research should further explore MUC1's biological mechanisms and its impact on therapy responses to solidify its use in clinical practice, aiming to improve outcomes for breast cancer patients.

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