Section: Pathology

Original Research Article

PROGNOSTIC SIGNIFICANCE OF MUC1 AND MUC2 EXPRESSION PATTERNS IN GASTRIC CARCINOMA: AN IMMUNOHISTOCHEMICAL ANALYSIS

A. Jayashree[1], S. Jenita Christiana Ranjana[2], G. Kayalvizhi[3]

[1]Assistant Professor, Department of Pathology, Thanjavur medical College, India.
[2]Professor, Department of Pathology, Government Ariyalur Medical College, India.
[3]Assistant Professor, Department of Pathology, Thanjavur Medical College, India.

Received : 11/01/2026
Received in revised form : 01/03/2026
Accepted : 16/03/2026

Keywords:
Gastric carcinoma. MUC1 and MUC2. Immunohistochemistry.

Corresponding Author:
Dr. S. Jenita Christiana Ranjana,
Email: jenitababu@gmail.com

DOI: 10.47009/jamp.2026.8.2.120

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (2); 645-649

ABSTRACT

Background: Gastric carcinoma is a biologically heterogeneous malignancy with variable clinical outcomes. Identification of reliable prognostic biomarkers is essential for risk stratification and personalized management. Altered expression of mucins, particularly MUC1 and MUC2, has been implicated in gastric tumor progression and prognosis. The objective is to evaluate the prognostic significance of MUC1 and MUC2 expression patterns in gastric carcinoma using immunohistochemistry and to correlate these findings with clinicopathological and prognostic parameters. **Materials and Methods:** This retrospective observational study included 45 histopathologically confirmed cases of gastric carcinoma. Immunohistochemical staining for MUC1 and MUC2 was performed on formalin-fixed paraffin-embedded tissue sections. Expression patterns were analyzed and correlated with clinicopathological parameters including tumor stage, nodal status, histological grade, lymphovascular invasion, perineural invasion, and TNM stage. Statistical analysis was carried out using appropriate tests, and a p-value of <0.05 was considered statistically significant. **Result:** MUC1 positivity was observed in 84.4% of cases and was significantly associated with advanced tumor stage, higher nodal involvement, poor differentiation, lymphovascular invasion, perineural invasion, and advanced TNM stage ($p < 0.05$). In contrast, MUC2 expression was observed in 66.7% of cases and showed a significant association with early-stage disease, limited nodal involvement, better histological differentiation, and favorable prognostic indicators ($p < 0.05$). Overall, MUC1 expression correlated with poor prognostic features, whereas MUC2 expression was associated with comparatively favorable tumor characteristics. **Conclusion:** The study highlights the prognostic utility of MUC1 and MUC2 expression patterns in gastric carcinoma. Combined immunohistochemical evaluation of these markers can serve as a valuable adjunct to routine histopathology for prognostic stratification and may aid in guiding individualized patient management strategies.

INTRODUCTION

Gastric carcinoma remains a major global health burden, ranking among the leading causes of cancer-related morbidity and mortality worldwide. Despite advances in diagnostic modalities and therapeutic strategies, the prognosis of gastric cancer continues to be poor, particularly in advanced stages, due to late presentation, biological heterogeneity, and high metastatic potential. Adenocarcinoma constitutes more than 90% of all gastric malignancies and exhibits diverse histopathological and molecular characteristics that significantly influence tumor behavior and patient outcomes. Hence, identification of reliable prognostic biomarkers is essential for improved risk stratification and personalized management.[1]

Mucins are high molecular weight glycoproteins produced by epithelial cells and play a crucial role in protecting the gastric mucosa by forming a viscoelastic barrier. Alterations in mucin expression patterns have been implicated in gastric carcinogenesis and tumor progression. Among the mucin family, MUC1 and MUC2 have gained considerable attention due to their contrasting biological functions and prognostic relevance. MUC1 is a transmembrane mucin that is normally expressed on the apical surface of epithelial cells. In

ISSN (O): 2687-5365; ISSN (P): 2753-6556

malignant transformation, loss of cellular polarity results in overexpression and aberrant distribution of MUC1 across the tumor cell surface, promoting tumor invasion, immune evasion, and metastatic spread by interfering with cell-cell adhesion mechanisms. Several studies have demonstrated an association between high MUC1 expression and advanced tumor stage, lymph node metastasis, and poor survival outcomes.[2]

In contrast, MUC2 is a secretory gel-forming mucin predominantly expressed in intestinal goblet cells and is typically absent in normal gastric mucosa. Its expression in gastric carcinoma is believed to reflect intestinal differentiation and is often associated with intestinal metaplasia, a recognized premalignant condition. Emerging evidence suggests that MUC2 expression may confer a protective effect by suppressing inflammation and limiting tumor aggressiveness, thereby correlating with early-stage disease and better prognosis. However, the exact role of MUC2 in gastric tumorigenesis remains controversial, with variable expression patterns reported across different populations.[3]

Immunohistochemistry (IHC) has become an indispensable tool in the evaluation of protein expression in tumor tissues, allowing precise localization and semi-quantitative assessment of biomarkers such as mucins. Studying the expression patterns of MUC1 and MUC2 using IHC provides valuable insight into tumor biology and facilitates correlation with clinicopathological parameters including tumor grade, stage, lymphovascular invasion, and nodal metastasis. Given the heterogeneity of gastric carcinoma and regional variations in disease characteristics, institution-based studies are essential to establish population-specific prognostic profiles.[4]

Aim: To evaluate the prognostic significance of MUC1 and MUC2 expression patterns in gastric carcinoma using immunohistochemistry.

Objectives

1. To assess the immunohistochemical expression of MUC1 and MUC2 in gastric carcinoma cases.
2. To correlate MUC1 and MUC2 expression patterns with clinicopathological parameters.
3. To determine the association of MUC1 and MUC2 expression with prognostic indicators of gastric carcinoma.

MATERIALS AND METHODS

Source of Data: The study data were obtained from histopathologically confirmed gastric carcinoma cases reported in gastrectomy specimens received in the Department of Pathology during the study period. Relevant clinical and pathological details were retrieved from hospital medical records and pathology registers.

Study Design: This was a retrospective observational analytical study conducted to evaluate immunohistochemical expression patterns of MUC1 and MUC2 in gastric carcinoma.

Study Location: The study was carried out in the Department of Pathology of a tertiary care teaching hospital.

Study Duration: The study was conducted over a period of two years.

Sample Size: A total of 45 histopathologically confirmed cases of gastric adenocarcinoma were included in the study.

Inclusion Criteria

- All gastrectomy specimens diagnosed as gastric carcinoma.
- Cases of gastric carcinoma irrespective of age and sex.
- Adequately preserved formalin-fixed paraffin-embedded tissue samples.

Exclusion Criteria

- Non-neoplastic and benign gastric lesions.
- Endoscopic biopsy specimens of gastric carcinoma.
- Gastrectomy specimens performed for non-malignant conditions.
- Inadequate or poorly preserved tissue samples.

Procedure and Methodology: Archived formalin-fixed paraffin-embedded tissue blocks of selected cases were retrieved. Hematoxylin and eosin-stained sections were reviewed to confirm diagnosis, tumor type, grade, and stage. Representative tumor sections were selected for immunohistochemical analysis. Clinicopathological parameters including age, sex, tumor site, tumor size, histological type, grade, lymphovascular invasion, perineural invasion, nodal status, and TNM staging were recorded for each case.

Sample Processing: Four-micron thick sections were cut from paraffin blocks and mounted on coated slides. Heat-induced antigen retrieval was performed. Immunohistochemical staining was carried out using rabbit monoclonal antibodies against MUC1 and MUC2 with polymer-based detection system. Diaminobenzidine was used as chromogen and hematoxylin as counterstain. Appropriate positive and negative controls were included in each batch.

Interpretation of Immunohistochemistry: MUC1 expression was evaluated based on membranous and cytoplasmic staining, while MUC2 expression was assessed based on cytoplasmic staining. Semi-quantitative scoring was performed according to the percentage of positive tumor cells and staining intensity, and categorized into negative, weak, moderate, and strong expression groups.

Statistical Methods: Data were analyzed using Statistical Package for Social Sciences (SPSS) software. Descriptive statistics were calculated. Association between categorical variables was assessed using Chi-square test or Fisher's exact test. A p-value of <0.05 was considered statistically significant.

Data Collection: Clinical details, histopathological findings, and immunohistochemical results were systematically recorded in a predesigned proforma. Data were compiled, verified, and analyzed to

ISSN (O): 2687-5365; ISSN (P): 2753-6556

establish correlations between mucin expression patterns and prognostic parameters.

RESULTS

[Table 1] shows the baseline clinicopathological characteristics of the study population comprising 45 gastric carcinoma cases. The mean age of patients was 53.1 ± 11.2 years, with a statistically significant deviation from the reference value ($p < 0.001$), indicating a predominance of middle-aged and elderly patients. Slightly more than half of the patients belonged to the ≥50 years age group (53.3%), while 46.7% were below 50 years; however, this age group distribution was not statistically significant ($p = 0.48$). A clear male predominance was observed, with males accounting for 62.2% of cases compared to 37.8% females, and this difference was statistically significant ($p = 0.02$). With respect to tumor size, the majority of cases (55.6%) had tumors larger than 6 cm, followed by tumors less than 3 cm (26.7%) and those measuring 3–6 cm (17.8%), and this distribution showed a significant association ($p = 0.01$), reflecting the tendency of gastric carcinoma to present at an advanced size. Regarding histological subtype based on Lauren classification, diffuse type carcinoma was slightly more common (53.3%) than intestinal type (46.7%); however, this difference was not statistically significant ($p = 0.31$).

Table 1: Baseline Clinicopathological Characteristics and Prognostic Significance (N = 45)

Parameter	Category	n (%) / Mean ± SD	95% CI	Test of significance	p value
Age (years)	—	53.1 ± 11.2	49.7 – 56.4	One-sample t-test	<0.001
Age group	<50 yrs	21 (46.7)	32.5–61.2	Chi-square	0.48
	≥50 yrs	24 (53.3)	38.8–67.5		
Sex	Male	28 (62.2)	46.5–76.2	Chi-square	0.02
	Female	17 (37.8)	23.8–53.5		
Tumor size	<3 cm	12 (26.7)	15.1–41.0	Chi-square	0.01
	3–6 cm	8 (17.8)	8.0–32.1		
	>6 cm	25 (55.6)	40.0–70.4		
Lauren type	Intestinal	21 (46.7)	32.5–61.2	Chi-square	0.31
	Diffuse	24 (53.3)	38.8–67.5		

Table 2: Immunohistochemical Expression of MUC1 and MUC2 in Gastric Carcinoma (N = 45)

Marker	Expression	n (%)	95% CI	Test of significance	p value
MUC1	Positive	38 (84.4)	70.5–93.5	One-sample proportion Z-test	<0.001
	Negative	7 (15.6)	6.5–29.5		
MUC2	Positive	30 (66.7)	51.6–79.6	One-sample proportion Z-test	0.02
	Negative	15 (33.3)	20.4–48.4		
MUC1 intensity	Strong (+++)	19 (42.2)	28.0–57.8	Chi-square	0.01
MUC2 intensity	Strong (+++)	11 (24.4)	13.1–39.7	Chi-square	0.04

[Table 2] summarizes the immunohistochemical expression patterns of MUC1 and MUC2 in gastric carcinoma. MUC1 expression was observed in a high proportion of cases, with 84.4% of tumors showing positivity, which was statistically significant ($p < 0.001$), highlighting its frequent overexpression in gastric malignancy. In contrast, MUC2 positivity was noted in 66.7% of cases and was also statistically significant ($p = 0.02$), though less prevalent than MUC1. When staining intensity was considered, strong MUC1 expression (+++) was observed in 42.2% of cases, showing a significant association ($p = 0.01$), whereas strong MUC2 expression was seen in 24.4% of tumors, which was also statistically significant ($p = 0.04$).

Table 3: Correlation of MUC1 and MUC2 Expression with Clinicopathological Parameters (N = 45)

Parameter	Category	MUC1 Positive n (%)	MUC2 Positive n (%)	Test of significance	p value
Tumor stage	Early (I–II)	9 (23.7)	17 (56.7)	Chi-square	0.003
	Advanced (III–IV)	29 (76.3)	13 (43.3)		
Nodal status	N0–N1	12 (31.6)	20 (66.7)	Chi-square	0.001
	N2–N3	26 (68.4)	10 (33.3)		
Histological grade	G1–G2	14 (36.8)	18 (60.0)	Chi-square	0.02
	G3	24 (63.2)	12 (40.0)		
Lauren type	Intestinal	20 (52.6)	18 (60.0)	Fisher exact	0.21
	Diffuse	18 (47.4)	12 (40.0)		

[Table 3] depicts the correlation between MUC1 and MUC2 expression and key clinicopathological parameters. MUC1 positivity was significantly higher in advanced tumor stages (III–IV), where 76.3% of cases were positive compared to only 23.7% in early stages (I–II), and this association was statistically significant ($p = 0.003$). Conversely, MUC2 expression was more frequently observed in early-stage tumors (56.7%) than in advanced stages (43.3%). A similar pattern was observed with nodal status, where MUC1 positivity was significantly higher in patients with advanced nodal disease (N2–N3) at 68.4%, compared to 31.6% in N0–N1 cases ($p = 0.001$). In contrast, MUC2 positivity was higher in

ISSN (O): 2687-5365; ISSN (P): 2753-6556

cases with limited nodal involvement (66.7% in N0–N1) and lower in advanced nodal disease (33.3%). With respect to histological grade, MUC1 expression was significantly associated with poorly differentiated tumors (G3), where 63.2% of cases were positive (p = 0.02), whereas MUC2 expression was more common in well to moderately differentiated tumors (60.0%). Although intestinal-type tumors showed slightly higher expression of both MUC1 (52.6%) and MUC2 (60.0%) compared to diffuse-type tumors, this difference was not statistically significant (p = 0.21).

Table 4: Association of MUC1 and MUC2 Expression with Prognostic Indicators (N = 45)

Prognostic indicator	Category	MUC1 Positive n (%)	MUC2 Positive n (%)	Test of significance	p value
Lymphovascular invasion	Present	26 (68.4)	9 (30.0)	Chi-square	<0.001
	Absent	12 (31.6)	21 (70.0)		
Perineural invasion	Present	18 (47.4)	7 (23.3)	Chi-square	0.01
	Absent	20 (52.6)	23 (76.7)		
TNM stage	Stage I–II	10 (26.3)	18 (60.0)	Chi-square	0.002
	Stage III–IV	28 (73.7)	12 (40.0)		
Overall prognostic trend	Poor	29 (76.3)	11 (36.7)	Fisher exact	<0.001
	Favorable	9 (23.7)	19 (63.3)		

[Table 4] illustrates the association of MUC1 and MUC2 expression with established prognostic indicators of gastric carcinoma. MUC1 positivity was significantly higher in tumors with lymphovascular invasion, with 68.4% of such cases showing positivity compared to 31.6% in tumors without lymphovascular invasion (p < 0.001). In contrast, MUC2 expression was more frequently observed in tumors without lymphovascular invasion (70.0%) than in those with invasion (30.0%). A similar trend was observed with perineural invasion, where MUC1 positivity was significantly higher in invasion-positive cases (47.4%) compared to invasion-negative cases (52.6%) (p = 0.01), while MUC2 positivity was predominantly seen in perineural invasion-negative tumors (76.7%). Furthermore, MUC1 expression was significantly associated with advanced TNM stage (III–IV), being present in 73.7% of such cases, whereas MUC2 expression was more common in early-stage disease (60.0%) (p = 0.002). When overall prognostic trends were analyzed, MUC1 positivity was significantly associated with poor prognostic outcomes (76.3%), while MUC2 positivity was predominantly associated with favorable prognostic features (63.3%) (p < 0.001).

DISCUSSION

The findings of the present study are in close agreement with previously published literature evaluating mucin expression patterns and their clinicopathological significance in gastric carcinoma. In the current cohort, the mean age of patients was 53.1 ± 11.2 years, with a predominance of cases above 50 years of age (53.3%). This age distribution is comparable to the observations reported by Yamini PM et al.(2025),[5] who documented peak incidence of gastric carcinoma in the fifth to sixth decades of life. The significant male predominance (62.2%) observed in this study is also consistent with global epidemiological trends reported by Hu LN et al.(2021),[3] attributing higher male incidence to differential exposure to risk factors such as smoking, dietary habits, and Helicobacter pylori infection. Furthermore, the majority of tumors in the present study were larger than 6 cm (55.6%), indicating late-stage presentation, a pattern similarly described by Radziejewska I. (2025),[4] who emphasized tumor size as an independent adverse prognostic factor. Although diffuse-type carcinoma slightly outnumbered intestinal-type tumors in the present series, the difference was not statistically significant, which aligns with the findings of Kerckhoffs KG et al.(2020),[6] who reported overlapping distributions of Lauren subtypes in Asian and developing populations.

Regarding immunohistochemical expression patterns, MUC1 positivity was observed in 84.4% of cases, demonstrating strong overexpression in gastric carcinoma. This high prevalence is comparable to reports by Ribeirinho-Soares S et al (2021),[7] who documented MUC1 expression rates ranging from 70% to 90% in gastric tumors and highlighted its association with tumor invasiveness and metastatic potential. The present study also demonstrated significant strong MUC1 staining intensity in 42.2% of cases, reinforcing the aggressive biological behavior linked to high MUC1 expression. In contrast, MUC2 positivity was observed in 66.7% of tumors, which is in accordance with the findings of Chen J et al (2025),[8] who reported MUC2 expression predominantly in intestinal-type and well-differentiated gastric carcinomas. The relatively lower proportion of strong MUC2 expression (24.4%) in the current study further supports the hypothesis that MUC2 is more frequently associated with differentiated phenotypes and less aggressive tumor behavior.

Correlation analysis revealed that MUC1 expression was significantly higher in advanced-stage tumors (76.3%), advanced nodal disease (68.4%), and poorly differentiated carcinomas (63.2%). Similar associations have been reported by Battista S et al (2021),[9] who demonstrated that MUC1 overexpression correlates with tumor depth, lymph node metastasis, and reduced overall survival. Conversely, MUC2 expression in the present study

ISSN (O): 2687-5365; ISSN (P): 2753-6556

was more frequent in early-stage tumors (56.7%), limited nodal involvement (66.7%), and well to moderately differentiated carcinomas (60.0%), which is consistent with observations by Wang S et al.(2025),[2] suggesting a protective or differentiation-associated role of MUC2. The lack of significant association between Lauren subtype and mucin expression in this study mirrors findings reported by Chelariu-Raicu A et al.(2022),[10] indicating that mucin expression patterns may transcend conventional histological classifications.

Furthermore, the association of MUC1 with adverse prognostic indicators such as lymphovascular invasion (68.4%), perineural invasion (47.4%), and advanced TNM stage (73.7%) observed in the present study corroborates earlier reports by Song K et al (2021),[11] who emphasized the role of MUC1 in promoting epithelial-mesenchymal transition, tumor cell motility, and metastatic dissemination. In contrast, MUC2 expression was predominantly observed in tumors without lymphovascular invasion (70.0%), absence of perineural invasion (76.7%), and early TNM stages (60.0%), supporting its association with favorable prognostic features, as also reported by Miao L et al.(2024).[12]

CONCLUSION

The present study demonstrates that immunohistochemical expression patterns of MUC1 and MUC2 have significant prognostic implications in gastric carcinoma. MUC1 expression was observed in a large proportion of cases and showed a strong association with adverse clinicopathological parameters such as advanced tumor stage, nodal metastasis, poor histological differentiation, lymphovascular invasion, perineural invasion, and advanced TNM stage. These findings support the role of MUC1 as a marker of aggressive tumor behavior and unfavorable prognosis. In contrast, MUC2 expression was more frequently associated with early-stage disease, limited nodal involvement, well to moderately differentiated tumors, absence of lymphovascular and perineural invasion, and overall favorable prognostic indicators. This inverse relationship between MUC1 and MUC2 expression patterns highlights their complementary roles in gastric carcinogenesis and tumor progression.

The combined assessment of MUC1 and MUC2 expression by immunohistochemistry provides valuable additional prognostic information beyond routine histopathological evaluation. Incorporation of these biomarkers into routine diagnostic practice may help in identifying high-risk patients who may benefit from closer surveillance and aggressive therapeutic strategies, as well as low-risk patients with comparatively better outcomes. Thus, MUC1 and MUC2 can be considered useful adjunct prognostic markers in gastric carcinoma and may contribute to more personalized patient management.

Limitations of the study

1. The sample size was relatively small (N = 45), which may limit the generalizability of the results.
2. The study was conducted at a single tertiary care center, which may introduce selection bias.
3. Being a retrospective study, complete clinical follow-up data and long-term survival outcomes were not available for correlation.
4. Inter-observer variability in immunohistochemical interpretation and scoring could not be completely eliminated.
5. Molecular and genetic profiling of tumors was not performed, which could have provided additional prognostic insights.
6. Only two mucin markers (MUC1 and MUC2) were evaluated, while other mucins such as MUC5AC and MUC6 were not included.
7. Treatment-related factors such as chemotherapy and radiotherapy response were not analyzed in relation to mucin expression.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556