ORIGINAL ARTICLE

Correlation of mucin1 expression with various grades and stages of colorectal carcinomas

Kezia Anna Jacob[1], Surekha U Arakeri[1]*

[1]Department of Pathology, BLDE (Deemed to be University), Shri B.M Patil Medical College Hospital and Research Centre, Vijayapura- 586103(Karnataka) India

Abstract

Background: Carcinoma of the colon and rectum is one of the commonest causes of cancer-related deaths globally. In India, the incidence of carcinoma of the colon and rectum is high due to genetic factors, lifestyle, and environmental factors. Over 50% of cases are diagnosed in the late stage, which leads to limitations in treatment and worsens prognosis. Biomarkers such as Carcinoembryonic Antigen and Mucin-1 (MUC1) play a crucial role as prognostic markers in Colorectal Carcinoma (CRC). Aim and Objectives: To evaluate and correlate MUC1 expression with the grading and staging of CRC. *Material and Methods:* A hospital-based cross-sectional study was done on 40 specimens received in the histopathology section of the department of pathology. Tumor tissue blocks on which diagnosis of CRC was made were evaluated for MUC1 expression and were correlated with grading and staging of CRC. *Results:* MUC1 expression showed score 3+ positivity in 70% cases of moderately differentiated adenocarcinoma, 50% cases of well-differentiated adenocarcinoma and in all cases of poorly differentiated adenocarcinoma. In 78.57% of T3 cases and 75% of T4 cases, score 3 MUC1 expression was observed. Score 3+ MUC1 expression was noted in 60% of N0, 82% of N1 and 100% of N2. The maximum number of cases showing the depth of invasion in the subserosa showed the highest score, that is, score 3, amounting to 85.71%. *Conclusion:* Overexpression of MUC1 is associated with the aggressiveness and progression of the tumor, and it can aid clinicians in intensifying chemotherapy in cases of CRC with high MUC1 expression.

Keywords: Colorectal Carcinoma, Immunohistochemistry, MUC1 Expression, Staging, Grading, Prognosis

Introduction

Around two million new cases of Colorectal Cancer (CRC), with approximately one million deaths, have been reported [1]. The National Cancer Registry data from 1982 to 2010 revealed a steady rise in the annual percentage change, ranging from 0.9% to 5.8% for carcinoma colon and 2.7% to 9.8% for carcinoma rectum. The latest report, based on 27 population-based cancer registries, indicated an annual incidence rate of 5.36 per one lakh population for carcinoma of the colon and 5.17 per one lakh for carcinoma of the rectum in men and in women [2].

The northeastern and southern regions of India have a much higher prevalence of colorectal cancer, potentially attributable to variations in genetic, lifestyle, and environmental variables. Notably, over 50% of colorectal carcinoma cases present at an advanced stage, which severely reduces the range of available treatments and deteriorates prognosis, ultimately resulting in high death rates [3]. Early detection and correct staging are important for improving patient outcomes. Present diagnostic modalities frequently fail to provide reliable prognostic insights [4]. Various biomarkers in CRC detection include Carcinoembryonic Antigen (CEA), CD133 and epithelial membrane antigen Mucin1 (MUC1). The glycoprotein CEA

has been widely recognized as a biomarker for colorectal cancer [5].

Among the potential biomarkers mentioned in the recent studies of CRC was MUC1. MUC1 is a transmembrane glycoprotein. It has been recognized for its significant aberrant expression in CRC. Also, it is associated with aggressive tumor behavior [6,7]. MUC1 expression studies have also been conducted on various malignant tumours, including ovarian, bladder, and thyroid tumours, by several authors [8,9,10]. A study on MUC1 expression in malignant ovarian tumors indicated that MUC1 is implicated in cancer progression and is also related to poor prognosis [8].

A study on bladder cancer indicated that MUC1 is crucial in preserving the mucosal integrity of the urothelium, and its abnormal expression contributes to the growth and spread of malignant bladder tumors [9]. In a study done on MUC1 expression in colorectal carcinoma, it was mentioned that MUC1 is indicative of poor prognosis. It also plays a role in epithelial-mesenchymal transition [11]. In some studies, a positive correlation between MUC1 and tumor grading was observed [12, 13]. The identification and evaluation of biomarkers such as MUC1 can help to plan treatment for CRC.

Material and Methods

Source of data

This hospital-based cross-sectional study was conducted on resected specimens of colorectal carcinoma received in the histopathology section of the Department of Pathology from 2019 to 2024. The study was approved by the Institutional Ethics Committee (BLDE (DU)/IEC/932/2023-24 dated 10.04.2023). All resected colorectal specimens diagnosed as carcinoma on histopathological examination were included in the study. Cases of colorectal carcinoma in which the tissue was inadequate for further immunohistochemical processing were excluded.

Methods of collection of data

Resected colorectal specimens, which were diagnosed as carcinoma on histopathology, were evaluated for grading and staging. Clinical details were collected from the patient's records. Evaluation of study cases was done under the headings of age, sex of the patient, tumor location, histological grading and staging of the tumor, depth of invasion, lymphovascular invasion and lymph node metastasis. Tumor tissue blocks on which diagnosis of carcinoma was done were evaluated for MUC1 expression. Then correlation of MUC1 expression was done with the grading and staging of CRC. For the immunohistochemistry study of MUC1, tissue sections 3 μm thick were placed on charged slides and incubated at 70°C for 20 minutes. Deparaffinization of the sections was done by two changes of xylene for 10 minutes each. Hydration of the sections was done by passing through absolute alcohol in 100%, 70%, 50% for 3 minutes each. Then, in distilled water for 3 minutes each. Sections were stored in Tris EDTA (pH 8.5 to 9.0) for antigen retrieval. Then, washed in distilled water for 3 minutes. After that slide was kept in 3% hydrogen peroxide for 10 minutes. Then, the sections were washed using a 0.05 mM Tris-buffered saline solution. Diluted mouse monoclonal antibodies targeting MUC1 were used as primary antibodies. Primary antibodies were applied to these sections and incubated for 45 minutes in a moist chamber. Tris-buffered saline solution (0.05mM) was used for washing. Then the target binder was added and incubated for 10 minutes. Then again, washed in Tris-buffered saline for 2 minutes. The sections were incubated with Polyexcel HRP for 10 minutes. Sections were treated with 0.5mg/ml 3, 3'-

diaminobenzidine solution. Hematoxylin was used for counterstaining. Slide mounting was completed after sections were cleaned in xylene and dried in ethanol. MUC1 Immunohistochemical (IHC) expression was evaluated and scored as follows: a score of 0 was assigned when no tumor cells exhibited MUC1 positivity. A score of 1+ was given when fewer than 10% of tumor cells showed positive staining. Cases in which 10–50% of tumor cells demonstrated MUC1 positivity were assigned a score of 2+, while a score of 3+ was recorded when more than 50% of tumor cells showed positive staining for MUC1 [14].

Sample size

The sample size was calculated using the formula described in the study by Kasprzak *et al*. (2018) [15]. Based on an anticipated correlation of 0.602 between the MUC1 expression levels of the two analyzed mucin transcripts, with a 95% confidence level and 98% power, the required sample size for the study was determined to be 40. Statistical analysis was performed using the Statistical Package for the Social Sciences (Version 20). Results were presented in a Microsoft Excel sheet. Categorical variables were compared using the Chi-square test. A p-value less than 0.05 was considered statistically significant.

Results

A total of 40 cases were evaluated for MUC1 expression in CRC. The age of the youngest patient was 28, and the oldest patient was 80 years old. The mean age of the study participants was 58 ± 13. The highest number of study participants was between 41 and 50 years, accounting for 27.5%, followed by those between 61 and 70 years and 71-80 years, which accounted for 22.5% of cases each. Gender wise distribution of CRC cases showed a mild female preponderance amounting to 57.5%.

The commonest clinical manifestation was of a detectable mass in the abdomen, summing up to 55%, followed by per rectal bleeding (20%), obstructive symptoms (15%) and abdominal pain (10%). The resected specimens of the study participants showed the most common gross presentation, with ulcero-proliferative growth accounting for 65%, followed by circumferential growth at 20%, exophytic growth at 10%, and polypoidal growth at 5%. The most common site involved was the rectum, accounting for 42.5%, followed by the colon at 35%, and the caecum at 22.5%. Adenocarcinoma was the predominant histological subtype, with 92.5%, followed by 5% of mucinous adenocarcinoma and 2.5% of signet ring cell carcinoma.

The grading of CRC showed that 82.5% of cases were moderately differentiated carcinomas, followed by 10% of cases that were well differentiated, and 7.5% of cases that were poorly differentiated. In poorly differentiated CRC, 2 cases were mucinous adenocarcinomas, and 1 case was a signet ring cell carcinoma. The maximum number of CRC cases were of T2 staging, amounting to 52.5%, followed by T3 (35%), T4 (10%) and T1 (2.5%). Out of 40 cases of CRC, 27.5% of cases showed metastasis in lymph nodes with N1 status, which is defined as one to three regional lymph node involvements. In 10% of cases, N2 status was noted, indicating involvement of more than four lymph nodes. When the association of grading was examined in conjunction with tumour staging, T3 staging was noted in all cases of poorly differentiated CRC. In contrast, the association between grading and staging was 25% and 30.30%, respectively, for well-differentiated and moderately differentiated CRC. When the correlation between the grading of the tumor and metastasis of lymph node was done, the highest percentage of metastasis in the N2 category was

noted in poorly differentiated CRC as compared to moderate and well-differentiated CRC, and the difference was statistically significant with a p-value of 0.007 (Table 1).

When the association of grading was done with depth of invasion, it was observed that in poorly differentiated CRC, the highest percentage of cases showed extension up to serosa and beyond serosa as compared to well differentiated CRC and moderately differentiated CRC, but the difference was statistically not significant (Table 2).

When the correlation of lymphovascular invasion was done with grading, it was observed that, as compared to well-differentiated and moderately differentiated CRC, the maximum number of cases showed lymphovascular invasion in poorly differentiated CRC. However, the difference was statistically not significant. When the correlation between metastasis in the lymph node and staging of CRC was done, stage 3 and stage 4 showed the highest percentage of metastasis compared to stage 1 and stage 2. However, the difference was not statistically significant. (Table 1).

When the correlation between staging and depth of invasion was studied, in stage T3 and T4, the highest number of cases showed the depth of invasion into serosa and subserosa compared to stage T1 and T2, and the difference was statistically significant (Table 2).

The correlation between staging and lymphovascular invasion showed that a larger number of cases in the T4 stage exhibited lymphovascular invasion compared to stages T1 to T3; however, the difference was statistically not significant (Table 2).

Overall, the evaluation of MUC1 expression in CRC cases showed a score of 1 in 3 cases (7.5%), a score of 2 in 9 cases, followed by a score of 3 in 28 cases (70%). In all cases of poorly differentiated CRC, score 3 MUC1 expression was noted. Score 3 MUC 1 expression was noted in a higher number of cases of moderately differentiated CRC as compared to well differentiated CRC, but the difference was statistically not significant. (Table 3, Figure 1-4 A&B)

Correlation of tumor staging with MUC1 expression showed a maximum number of cases showing score 3 expression in stage T3 and T4 amounting to 78.57 % and 75% respectively. All cases of stage T1 showed score 1 MUC1 expression and the difference between various tumor staging with MUC1 expression score was statistically significant (Table 3).

The score 3 MUC1 expression was highest in CRC cases with N2 category lymph node metastasis, amounting to 100%, and lowest in the N0 category, amounting to 60%. However, the difference was statistically not significant (Table 3).

When the association of depth of invasion and MUC1 expression was done, a maximum number of cases showing the depth of invasion in subserosa showed the highest score that is score 3, amounting to 85.71%. Score 3 MUC1 expression was not observed in cases of CRC limited to submucosa and difference between depth of invasion and MUC1 expression score was statistically significant. (Table 3)

When the association between lymphovascular invasion and MUC1 expression was done, score 3 MUC1 expression was higher in cases showing lymphovascular invasion as compared to CRC cases without lymphovascular invasion, but the difference was not statistically significant. (Table 3)

When the association between the site of CRC and MUC1 expression was studied, score 3 expression of MUC1 was noted in 88.8% of CRC cases of the caecum, followed by 71.4% of colon and 58.8% of rectum. However, the difference was not significant

statistically. The association of gross morphology in CRC and MUC1 expression showed, score 3 expression of MUC1 in 100% of CRC cases presented with polypoidal growth followed by 73.07% ulceroproliferative growth and 62.5% circumferential growth, but the difference was statistically not significant.

Discussion

A distinguishing feature of CRC is its capacity to secrete mucin. Usually, the mucin protects epithelial surfaces by lubricating the surface of the epithelium [12]. MUC1 is crucial in preserving the mucosal integrity, and its abnormal expression can contribute to the progression and spread of malignant tumors [9]. MUC1 expression studies done on various malignant tumors mentioned that MUC1 is implicated in cancer progression [8-10]. The maximum number of study participants was within the age group of 41 to 50 years. These findings in the present study are in concordance with the results of Kesari *et al*. (2015) [12]. The incidence of CRC was slightly higher in males as compared to females. It was mentioned that sex steroid hormones and microbiota of the gastrointestinal tract may be the cause of it [12]. However, in the present study, a mild female preponderance was noted, amounting to 42.5% males and 57.5% females.

The clinical symptoms of CRC vary across different anatomical regions in the colon and rectum, due to their distinct anatomical and physiological functions. Typically, abdominal pain and systemic symptoms are prevalent in right colon cancer, while hematochezia and obstruction are more frequent in left colon cancer, and alterations in defecation habits are more characteristic of rectal cancer [16]. Kesari *et al*. (2015) [12] noted blood in stool in 66%, pain in the abdomen and a mass in the abdomen in 48% of cases, and changed bowel habits in 43% of cases of CRC. It was also mentioned that ulceroproliferative growth was found in 48% of cases of CRC.

The most common site involved in our study was the rectum, accounting for 42.5%, followed by the colon (35%) and the caecum (22.5%). In the same way, Kesari *et al*. (2015) [12] found that CRC most

Table 1: Association of grading and staging of CRC with lymph node metastasis

Grading	**N0**	**N1**	**N2**	**Chi-square**	***p***
WD CRC (n=4)	4 (100%)	0 (0.0%)	0 (0.0%)	14.206	*0.007
MD CRC (n=33)	20(60.61%)	11(33.33%)	2 (6.06%)		
PD CRC (n=3)	1 (33.33%)	0 (0.0%)	2(66.67%)		
Staging					
T1 (n=01)	1 (100%)	0 (0.0%)	0 (0.0%)	3.5	0.73
T2 (n=21)	16(76.19%)	4 (19.04%)	1 (4.76%)		
T3 (n= 14)	7 (50%)	5 (35.71%)	2(14.28%)		
T4 (n= 4)	1 (25%)	2 (50%)	1 (25%)		

Table 2: Association of grading of CRC with depth of invasion & association of staging of CRC with depth of invasion and lymphovascular invasion

Grading	**Depth of invasion**				**Chi-square**	***p***
	Subserosa (n=7)	**Serosa (n=12)**	**Muscularis propria (n=20)**	**Submucosa (n=1)**		
WD CRC (n=4)	0 (0.0%)	2 (50%)	2 (50%)	0 (0.0%)	5.229	0.51
MD CRC(n=33)	6 (18.19%)	8 (24.24%)	18 (54.54%)	1 (3.03%)		
PD CRC(n=3)	1 (33.33%)	2 (66.67%)	0 (0.0%)	0 (0.0%)		
Staging	**Depth of invasion**					
T1(n=1)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100%)	20.85	*0.013
T2(n=21)	2 (9.52%)	3 (14.29%)	16 (76.19%)	0 (0.0%)		
T3(n=14)	5 (35.71%)	6 (42.86%)	3 (21.43%)	0 (0.0%)		
T4 (n= 4)	0 (0.0%)	3 (75%)	1 (25%)	0 (0.0%)		
Staging	**Lymphovascular Invasion**					
	Yes (n=14)		No (n=26)			
T1(n=1)	0(0.0%)		1 (100%)		1.63	0.65
T2(n=21)	6(28.57%)		15(71.43%)			
T3(n=14)	5(35.71%)		9(64.29%)			
T4 (n= 4)	3(75%)		1(25%)			

Table 3: Association of grading, staging, lymph node metastasis, depth of invasion & lymphovascular invasion of CRC with MUC1 expression

Grading	**Score 1**	**Score 2**	**Score 3**	**Chi- square**	***p***
WD CRC (n=4)	1(25%)	1(25%)	2(50%)	3.29	0.51
MD CRC (n=33)	2(6.06%)	8(24.24%)	23(69.70%)		
PD CRC (n=3)	0(0.0%)	0(0.0%)	3(100%)		

Continued...

Tumor Staging					
T1 (n=1)	1(100%)	0(0.0%)	0(0.0%)	13.81	*0.032
T2(n=21)	1(4.76%)	6(28.57%)	14(66.67%)		
T3 (n=14)	1(7.14%)	2(14.29%)	11(78.57%)		
T4 (n=4)	0(0.0%)	1(25%)	3(75%)		
Lymph Node Metastasis					
N0 (n=25)	3(12%)	7(28%)	15(60%)	4.218	0.377
N1 (n=11)	0(0.0%)	2(18.18%)	9(81.82%)		
N2 (n=4)	0(0.0%)	0(0.0%)	4(100%)		
Depth of invasion					
Subserosa (n=7)	0(0.0%)	1(14.29%)	6(85.71%)	13.601	*0.034
Serosa (n=12)	1(8.33%)	3(25%)	8(66.67%)		
Muscularis propria (n=20)	1(5%)	5(25%)	14(70%)		
Submucosa (n=1)	1(100%)	0(0.0%)	0(0.0%)		
Lymphovascular invasion					
Yes (n=14)	1(7.14%)	2(14.29%)	11(78.57%)	0.876	0.645
No (n=26)	2(7.70%)	7(26.92%)	17(65.38%)		

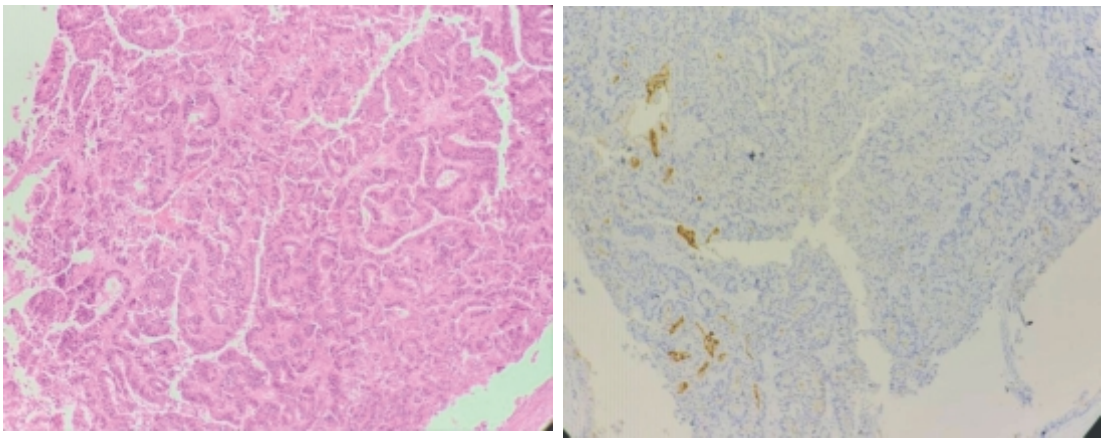

Figure 1: Photomicrograph showing well differentiated adenocarcinoma of MUC1 expression, score 1 (AH & E, B- IHC, 100×)

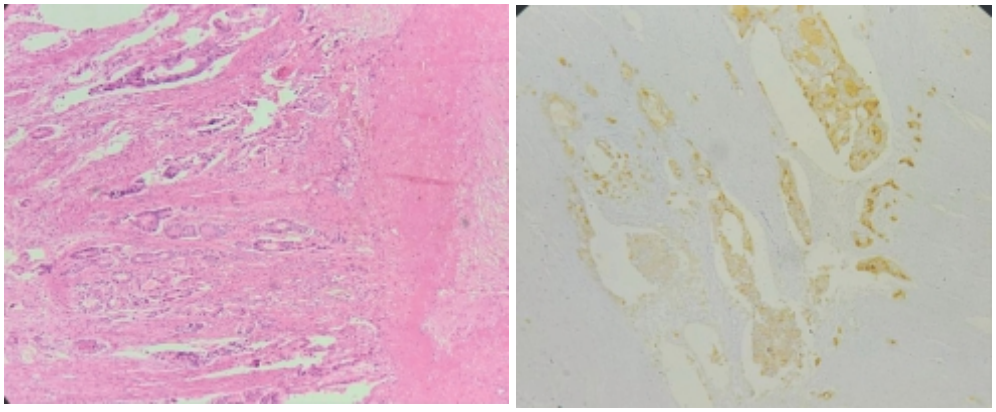

Figure 2: **Photomicrograph showing moderately differentiated adenocarcinoma of MUC1 expression, score 2 (A – H & E, B- IHC, 100×)**

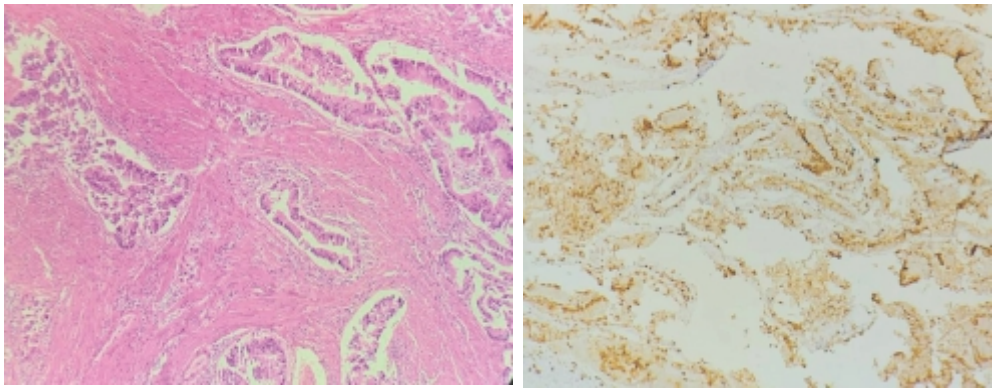

Figure 3: **Photomicrograph showing moderately differentiated adenocarcinoma of MUC1 expression score 3 (A – H & E, B - IHC, 100×)**

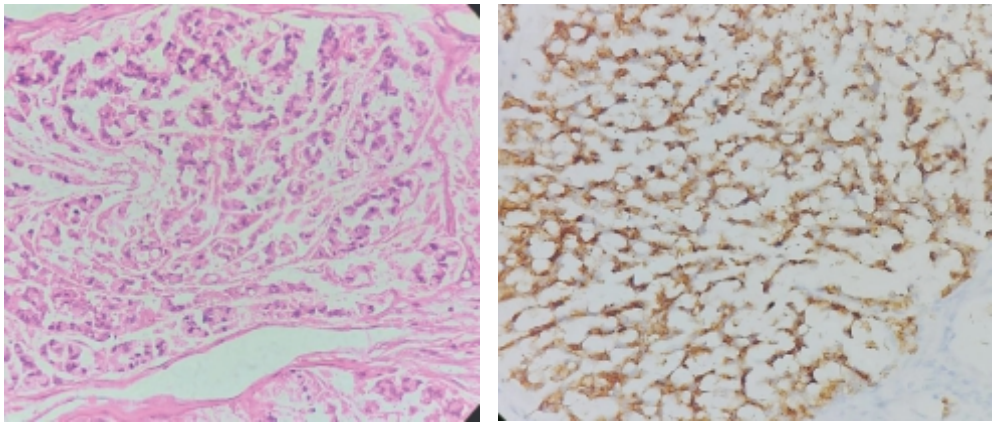

Figure 4: **Photomicrograph showing poorly differentiated Signet ring cell carcinoma of MUC1 expression score 3 (A – H & E, B - IHC, 100×)**

often occurred in the rectum and ascending colon, accounting for 30% each. This was followed by the sigmoid colon in 26%, the descending colon in 8%, and the transverse colon in 6% of cases. In the present study, adenocarcinoma was the predominant histological subtype, accounting for 92.5%, followed by 5% of mucinous adenocarcinoma and 2.5% of signet ring cell carcinoma.

Similar observations were noted in a study by Debbarma *et al*. (2023) [17] and Duncan *et al*. (2007) [18], and Ekta *et al*. (2007) [19] which showed that adenocarcinoma was the predominant histological subtype. The majority of the cases in the present study were moderately differentiated, followed by well-differentiated and poorly differentiated CRC. Similarly, Debbarma *et al*. (2023) [17] also noted that the majority of the tumours were moderately differentiated, followed by poorly differentiated.

The maximum number of cases were of pT stage T2, amounting to 52.5% followed by T3 (35%), T4 (10%) and T1 (2.5%). Similarly, in a study by Kesari *et al*. (2015) [12], 46% of cases were in stage pT2, followed by the pT3 stage in 44 % of cases, pT stage 1 in 6 % of cases, and stage 4 in 4 % of cases of CRC. These findings are similar to the findings of the present study, with the maximum number of cases in the pT2 stage. In the indexed study, out of the 40 cases studied, 62.5% did not show any lymph node involvement, followed by N1 cases, amounting to 27.5%, followed by N2 cases (10%). On the contrary, Díaz *et al*. (2018) [13] noted that lymph node metastases occurred in 39.6% of the cases with N1 status, in 22.1% of % N1 cases and N2 status in 14.8% of % N2 cases.

Four patients in our study with well-differentiated CRC showed N0 lymph node involvement. Out of 33 patients with moderately differentiated CRC, 20 (60.6%) showed N0 lymph node involvement, 11 (33.3%) showed N1 lymph node involvement and two patients (6.06%) showed N2 involvement. Out of 3 patients with poorly differentiated CRC, 1 (33.3%) showed N0 lymph node involvement, and two patients (66.6%) showed N2 involvement ($p = 0.007$). In a study done by Derwinger *et al*. (2010) [20] on 1239 patients who underwent surgical resection for colorectal cancer, a substantial correlation was demonstrated between tumor grading and T-stage, as well as the risk of lymph node metastasis ($p < 0.001$). The higher grade correlated with an increased positive lymph node count in stage III illness ($p < 0.001$).

Depth of submucosal invasion is considered as an important predictive factor for lymph node metastasis. One patient in present study with T1 stage had submucosal involvement. Out of 21 patients with stage T2, subserosal involvement was seen in two patients (9.52%), three patients (14.28%) showed involvement of serosa, and 16 patients (76.19%) showed muscularis propria involvement. Out of 14 patients with stage T3, subserosal involvement was seen in five patients (35.71%), six patients (42.85%) showed serosa involvement, and three patients (21.42%) showed muscularis propria involvement. Out of 4 patients with T4 stage CRC, 3 patients (75%) showed serosa involvement, and one patient (100%) showed muscularis propria involvement. The association of staging with depth of invasion was statistically significant ($p = 0.013$). Foersch *et al*. (2022) [21] observed that tumors with pT3b, which have an infiltration depth of more than 3 mm, showed a worse prognosis compared to pT3a tumors in which invasion of tumor tissue into the adipose tissue was 3 mm or less. The association of tumor staging of CRC and MUC1 expression in the present study showed score 3 MUC1 expression in

more cases of CRC with T3 and T4 stages, as compared to T1 and T2 stages, with a statistically significant difference (p = 0.03). Similar observations were noted in a study done by Yu *et al*. (2007) [22]. In the present study, association of grading with MUC1 expression showed score 3 MUC1 expression in all cases of poorly differentiated adenocarcinoma, but the difference was statistically insignificant. These observations were similar to Khemeri *et al*. (2019) [23] study, which showed that on comparing low grade (G1) with high grade G2/G3 tumors, the high grade-tumors showed significantly stronger MUC1 expression. In the present study, when the association between lymph node metastasis and MUC1 expression was done, the highest number of CRC cases, with N2 and N1, showed a higher percentage of CRC with a score of 3 for MUC1 expression. However, the difference was statistically not significant. A study by Aisawa *et al*. (2024) [24] revealed that 38.8% of MUC1-positive colorectal tumors demonstrated lymph node metastasis in contrast to MUC1-negative tumors. Increased frequency of lymph node metastases in MUC1-positive cases suggests that MUC1-mediated pathways may promote the migration of carcinoma cells to lymph nodes through stromal lymphatic channels [24]. There was a positive association between depth of invasion and MUC1 expression, with a statistically significant difference, (p = 0.03). Similarly, in the study done by Aisawa *et al*. (2024) [23], 26 cases showed positive MUC1 expression, among which highest number of cases showed depth of invasion beyond serosa and the difference was statistically significant. In a study by Betge *et al.* (2016) [25], 13% of cases with high MUC1 expression showed lymphovascular invasion, while 56% of cases with low MUC1 expression exhibited lymphovascular invasion. The association between lymphovascular invasion and MUC1 expression was not significant in our study.

Conclusion

MUC1 expression was high in cases of CRC with advanced stages and in cases with a depth of invasion extending beyond the serosa and subserosa. Also, score 3 MUC1 expression was more in cases of CRC showing poorly differentiated carcinoma and in CRC cases with lymph node metastasis and lymphovascular invasion. These findings suggest that a high MUC1 score leads to the interruption of cell adhesion, which in turn facilitates metastasis and invasion. Based on this, we conclude that MUC1 expression may be upregulated in CRC. This effect of MUC1 may cause the progression of tumor and the aggressiveness of CRC, and it can help in guiding clinicians to intensify chemotherapy in cases of CRC with high MUC1 expression. In cases of metastatic or unresectable CRC, MUC1-based immunotherapy can also be developed to overcome the limited treatment options. It also opens avenue for MUC1-specific CAR-T cell therapy and specific anti MUC1 antibody probes for targeted therapy. However, further multicenter studies are needed with a larger sample size to validate the study's observations.

References

1. Morgan E, Arnold M, Gini A, Lorenzoni V, Cabasag CJ, Laversanne M, *et al*. Global burden of colorectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCAN. *Gut* 2023; 72(2):338-44.
2. Asthana S, Khenchi R, Labani S. Incidence of colorectal cancers in India: A review from population-based cancer registries. *Curr Med Res Pract* 2021; 11(2):91-96.
3. Gonzalez-Pons M, Cruz-Correa M. Colorectal cancer biomarkers: where are we now?. *Biomed Res Int* 2015: 2015:149014.
4. Zhang Y, Wang Y, Zhang B, Li P, Zhao Y. Methods and biomarkers for early detection, prediction, and diagnosis of colorectal cancer. *Biomed Pharmacother* 2023; 163:114786.
5. Beauchemin N, Arabzadeh A. Carcinoembryonic Antigen-related Cell Adhesion Molecules (CEACAMs) in cancer progression and metastasis. *Cancer Metastasis Rev* 2013; 32(3-4):643-671.
6. Li C, Liu T, Yin L, Zuo D, Lin Y, Wang L. Prognostic and clinicopathological value of MUC1 expression in colorectal cancer: A meta-analysis. *Medicine (Baltimore)* 2019; 98(9):e14659.
7. Zhang Y, Dong X, Bai L, Shang X, Zeng Y. MUC1-induced immunosuppression in colon cancer can be reversed by blocking the PD1/PDL1 signaling pathway. *Oncol Lett* 2020; 20(6):317.
8. Hu XF, Yang E, Li J, Xing PX. MUC1 cytoplasmic tail: a potential therapeutic target for ovarian carcinoma. *Expert Rev Anticancer Ther* 2006; 6(8):1261-71.
9. Kaur S, Momi N, Chakraborty S, Wagner DG, Horn AJ, Lele SM, *et al*. Altered expression of transmembrane mucins, MUC1 and MUC4, in bladder cancer: pathological implications in diagnosis. *PLoS One* 2014; 9(3):927-42.
10. Baek SK, Woo JS, Kwon SY, Lee SH, Chae YS, Jung KY. Prognostic significance of the MUC1 and MUC4 expressions in thyroid papillary carcinoma. *Laryngoscope* 2007; 117(5): 911-916.
11. Khanh DT, Mekata E, Mukaisho KI, Sugihara H, Shimizu T, Shiomi H, *et al*. Transmembrane mucin MUC1 overexpression and its association with CD 10+ myeloid cells, transforming growth factor-β1 expression, and tumor budding grade in colorectal cancer. *Cancer Sci* 2013;104(7): 958-964.
12. Kesari MV, Gaopande VL, Joshi AR, Babanagare SV, Gogate BP, Khadilkar AV. Immunohistochemical study of MUC1, MUC2 and MUC5AC in colorectal carcinoma and review of literature. *Indian J Gastroenterol* 2015; 34(1): 63-67.
13. Díaz Del Arco C, Garré P, Molina Roldán E, Lorca V, Cerón Nieto MÁ, Fernández Aceñero MJ. MUC1 expression in colorectal carcinoma: clinicopathological correlation and prognostic significance. *Revista Española de Patología* 2018; 51(4):204-209.
14. Raj N, Kumar A, Rai P, Rao RN. MUC1 expression in gastric adenocarcinomas: its prognostic significance and clinicopathological correlation. *Acta Sci Gastroint Disord* 2021; 4(4):20-27
15. Kasprzak A, Siodła E, Andrzejewska M, Szmeja J, Seraszek-Jaros A, Cofta S, *et al*. Differential expression of mucin 1 and mucin 2 in colorectal cancer. *World J Gastroenterol* 2018; 24(36):4164-4177.
16. Skalitzky MK, Zhou PP, Goffredo P, Guyton K, Sherman SK, Gribovskaja-Rupp I, et al. Characteristics and symptomatology of colorectal cancer in the young. *Surgery* 2023; 173(5):1137-1143.
17. Debbarma B, Singh O, Singh GC, Konsam C, Rai P, Debbarma D. Mucin1 Expression in relation to histomorphological type of colorectal carcinoma: A cross sectional study. *Int J Adv Res* 2023; 11(12):302-308.
18. Duncan TJ, Watson NF, Al-Attar AH, Scholefield JH, Durrant LG. The role of MUC1 and MUC3 in the biology and prognosis of colorectal cancer. *World J Surg Oncol* 2007; 5:31.
19. Ekta, Bansal N, Roychoudhury AK, Shaffy. A Histopathological Spectrum of Gastrointestinal Tract Lesions in a Tertiary Care Centre in South Western Part of India: An Epidemiological Study. *J Krishna Inst Med Sci Univ* 2018:7(3): 43-47.
20. Derwinger K, Kodeda K, Bexe-Lindskog E, Taflin H. Tumour differentiation grade is associated with TNM staging and the risk of node metastasis in colorectal cancer. *Acta oncologica* 2010; 49(1):57-62.
21. Foersch S, Lang-Schwarz C, Eckstein M, Geppert C, Schmitt M, Konukiewitz B, *et al*. pT3 colorectal cancer revisited: a multicentric study on the histological depth of invasion in more than 1000 pT3 carcinomas—proposal for a new pT3a/pT3b subclassification. *Br J Cancer* 2022; 127(7):1270-1278.
22. Yu XW, Rong W, Xu FL, Xu GY, Sun YR, Feng MY. Expression and clinical significance of Mucin and E-cadherin in colorectal tumors. *Ai Zheng* 2007; 26(11):1204-1210.
23. Khemiri M, Doghri R, Mrad K, Friedrich K, Oueslati R. Mucin-1 expression and localization in epithelial cells shows characteristic and distinct patterns in inflammatory bowel diseases and colorectal cancer. *Int J Clin Exp Pathol* 2019; 12(5):17-31.

24. Aisawa H, Yoshizawa T, Goto S, Chiba H, Morohashi S, Hakamada K. Mucin Expression Patterns of Human Colorectal Adenocarcinoma. *Biomed Res J* 2024; 6(3):531-535.

25. Betge J, Schneider NI, Harbaum L, Pollheimer MJ, Lindtner RA, Kornprat P, *et al*. MUC1, MUC2, MUC5AC, and MUC6 in colorectal cancer: expression profiles and clinical significance. *Virchows Archiv* 2016; 469(3): 255-265.

Author for Correspondence:
Dr. Surekha. U. Arakeri, Department of Pathology, BLDE (Deemed to be University), Shri B.M Patil Medical College Hospital and Research Centre, Vijayapura- 586103, Karnataka Email: surekha.arakeri@bldedu.ac.in
Cell: 984576844

How to cite this article:
Jacob KA, Arakeri SU. Correlation of mucin1 expression with various grades and stages of colorectal carcinomas. *J Krishna Inst Med Sci Univ* 2025; 14(4): 29-40

Submitted: *29-June-2025* ***Accepted:*** *02-Sep-2025* ***Published:*** *01-Oct-2025*