Section: Pathology

Original Research Article

A STUDY OF COLORECTAL NEOPLASMS WITH KI67 EXPRESSION IN A TERTIARY CARE CENTRE

Madhurima Bhattacharyya[1], Prasit Kumar Ghosh[2], Utpal Goswami[3]

[1-3]Department of Pathology, ICare Institute of Medical Sciences & Research Haldia, West Bengal, India.

Received : 10/01/2026
Received in revised form : 21/02/2026
Accepted : 09/03/2026

Keywords:
Colorectal cancer, Ki-67, Immunohistochemistry, Tumor proliferation, Histopathological grade, TNM stage.

Corresponding Author:
Dr. Madhurima Bhattacharyya,
Email: m.bhattacharyya@gmail.com

DOI: 10.47009/jamp.2026.8.2.133

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

Int J Acad Med Pharm
2026; 8 (2); 710-717

ABSTRACT

Background: Colorectal cancer is a biologically heterogeneous malignancy with variable clinical outcomes, even among tumors of similar histopathological grade and stage. Conventional prognostic parameters alone are often insufficient to predict tumor behavior. Ki-67, a nuclear proliferation marker, has been widely studied in several malignancies; however, its prognostic relevance in colorectal neoplasms remains controversial. **Objective:** To evaluate Ki-67 expression in colorectal neoplasms and to determine its correlation with histopathological grade and pTNM stage of colorectal adenocarcinoma. **Materials and Methods:** This prospective observational study was conducted in the Department of Pathology at a tertiary care center over an 18-month period. A total of 52 histologically diagnosed cases of colorectal neoplasms were included. Clinical details, gross and microscopic findings, and pathological risk factors were documented. Immunohistochemical staining for Ki-67 was performed, and the Ki-67 labeling index was assessed based on the percentage of positively stained tumor nuclei. Statistical analysis was carried out to evaluate the association of Ki-67 expression with histopathological grade and tumor stage. **Results:** The mean age of patients was 57.03 ± 11.33 years, with a male predominance (male-to-female ratio 2.5:1). Adenocarcinoma constituted 90.4% of cases, with moderately differentiated adenocarcinoma being the most common subtype (71.2%). High Ki-67 expression was predominantly observed in malignant tumors and showed a progressive increase with higher histopathological grade and advanced pTNM stage. Tumors with adverse pathological features such as lymphovascular invasion, perineural invasion, and nodal metastasis demonstrated higher Ki-67 labeling indices. **Conclusion:** Ki-67 expression correlates positively with histopathological grade and tumor stage in colorectal adenocarcinoma, reflecting increased tumor proliferative activity and biological aggressiveness. Ki-67 may serve as a valuable adjunct marker to conventional histopathological parameters for improved risk stratification in colorectal cancer.

INTRODUCTION

Colorectal cancer (CRC) represents a significant global health challenge and is one of the most frequently diagnosed malignancies worldwide. It ranks as the third most common cancer and the second leading cause of cancer-related mortality, accounting for a substantial proportion of cancer deaths annually.[1] Although improvements in screening programs, surgical techniques, and adjuvant therapies have reduced mortality in several regions, patient outcomes remain heterogeneous, even among individuals with similar histopathological grade and TNM stage.[2] This variability highlights the limitations of conventional prognostic parameters and underscores the importance of identifying additional biomarkers that better reflect tumor biology.

Tumor cell proliferation is a key determinant of cancer progression and aggressiveness. Ki-67 is a nuclear protein expressed in all active phases of the cell cycle except G0 and is widely used as an immunohistochemical marker of cellular proliferation.[3] The Ki-67 labeling index has demonstrated prognostic and predictive value in multiple malignancies, including breast carcinoma and neuroendocrine tumors.[4] However, the clinical significance of Ki-67 expression in colorectal neoplasms remains controversial. While some studies have reported associations between high Ki-67

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

expression and advanced tumor grade or stage, others have shown favorable outcomes in tumors with high proliferative indices, particularly in patients receiving adjuvant chemotherapy.[5,6] Therefore, this study aims to evaluate Ki-67 expression in colorectal neoplasms and correlate it with histopathological grade and TNM stage of colorectal adenocarcinoma.

Objective: To evaluate the expression of Ki-67 in colorectal neoplasms and to determine its correlation with histopathological grade and TNM stage of colorectal adenocarcinoma.

MATERIALS AND METHODS

This institution-based prospective observational study was conducted in the Department of Pathology at ICARE Institute of Medical Sciences and Research, Haldia, West Bengal, over an 18-month period from July 2023 to December 2024, after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to inclusion in the study. Histologically diagnosed cases of colorectal neoplasms received as colonoscopic biopsies, endoscopic biopsies, or surgical resection specimens were included. Specimens that were inadequate, non-representative, or composed predominantly of necrotic tissue, as well as cases without consent, were excluded. Based on institutional case availability during the study period, a total of 52 cases were enrolled.

All specimens were fixed in 10% neutral buffered formalin within 30 minutes of receipt and processed according to standard histopathological protocols. Paraffin-embedded tissue sections of 4 µm thickness were prepared and stained with hematoxylin and eosin for routine microscopic examination. Histopathological evaluation was performed to determine tumor type, histological grade, depth of invasion, lymph node status, and TNM stage in accordance with established classification systems.

Immunohistochemical staining for Ki-67 was performed on representative tumor sections using standard immunohistochemistry techniques. Sections of 1 µm thickness were cut, mounted on charged slides, and subjected to antigen retrieval followed by incubation with primary Ki-67 antibody. Nuclear staining of tumor cells was considered positive. The Ki-67 labeling index was calculated as the percentage of positively stained tumor cell nuclei among at least 1,000 tumor cells counted in areas of highest staining intensity under high-power magnification.

Clinicopathological data and immunohistochemical findings were recorded systematically. Statistical analysis was performed using appropriate statistical software. Categorical variables were analyzed using chi-square or Fisher's exact test, and correlations between Ki-67 expression and histopathological grade and TNM stage were assessed using correlation analysis. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1: Baseline Demographic and Anthropometric Characteristics of the Study Population (n = 52)

Variable	Category / Parameter	Frequency / Mean	Percentage (%) / SD
Age (years)	31–40	3	5.8
	41–50	11	21.2
	51–60	19	36.5
	61–70	13	25.0
	>70	6	11.5
	Mean age (years)	**57.03**	**±11.33**
Sex	Male	37	71.2
	Female	15	28.8
	Male : Female ratio	**2.5 : 1**	—
Religion	Hindu	36	69.2
	Muslim	16	30.8
	Hindu : Muslim ratio	**2.25 : 1**	—
Anthropometry	Height (cm)	160.01	±4.98
	Weight (kg)	57.01	±5.51
	BMI (kg/m²)	22.33	±2.39

The study population comprised 52 participants with a mean age of 57.03 ± 11.33 years, with the largest proportion (36.5%) belonging to the 51–60-year age group. Males predominated, accounting for 71.2% of cases, with a male-to-female ratio of 2.5:1. The majority of participants were Hindu (69.2%), while Muslims constituted 30.8% of the study population. The mean height, weight, and body mass index were 160.01 ± 4.98 cm, 57.01 ± 5.51 kg, and 22.33 ± 2.39 kg/m², respectively.

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

Table 2: Distribution of Clinical Features (n=52)

Clinical Features	Type	Frequency	Percentage
Altered Bowel Habits	Yes	37	71.2
	No	15	28.8
Rectal Bleeding	Yes	24	46.2
	No	28	53.8
Anaemia	Yes	20	38.5
	No	32	61.5
Abdominal Pain	Yes	37	71.2
	No	15	28.8
Unintentional Weight Loss	Yes	28	53.8
	No	24	46.2
Family History cancer positivity	Yes	6	11.5
	No	46	88.5
Obesity	Yes	8	15.4
	No	44	84.6
Diet	Vegetarian	5	9.6
	Non-vegetarian	47	90.4
Cigarette Smoking	Yes	18	34.6
	No	34	65.4
Alcohol consumption	Yes	7	13.5
	No	45	86.5

In the study population of 52 individuals, altered bowel habits and abdominal pain were reported by 71.2% of participants each. Rectal bleeding was observed in 46.2%, while unintentional weight loss was noted in 53.8%. Anaemia was present in 38.5% of the cases. A family history of cancer was positive in 11.5%, and obesity was reported by 15.4%. Regarding lifestyle factors, 90.4% of the participants consumed a non-vegetarian diet, while only 9.6% were vegetarian. Cigarette smoking was prevalent among 34.6%, and alcohol consumption was reported by 13.5% of the study group.

Table 3: Type of specimen (n=52)

Type of specimen	Frequency	Percentage
Colonoscopic biopsy	15	28.8
Anterior resection	15	28.8
Right hemicolectomy	5	9.6
Right hemicolectomy with mid transverse colectomy	4	7.7
Right hemicolectomy with right transverse colectomy	3	5.8
Punch biopsy	3	5.8
Sigmoidoscopy biopsy	3	5.8
Sigmoidectomy	3	5.8
Incisional biopsy	1	1.9
Total	52.0	100.0

The types of specimens collected varied, with colonoscopic biopsies and anterior resections each comprising 28.8% of the samples. Right hemicolectomies accounted for 9.6%, while right hemicolectomies combined with mid transverse colectomies made up 7.7%. Both right hemicolectomies with right transverse colectomies and punch biopsies were reported in 5.8% of cases, as were sigmoidoscopy biopsies and sigmoidectomies. Incisional biopsies were the least common, constituting only 1.9% of the specimens.

Table 4: Location of Neoplasm (n=52)

Location of Neoplasm	Frequency	Percentage
Rectum	14	26.9
Recto-sigmoid junction	10	19.2
Ascending colon	7	13.5
Recto-sigmoid junction, sigmoid colon	6	11.5
Ascending colon, Caecum	5	9.6
Sigmoid colon	4	5.8
Transverse colon	3	7.7
Descending colon	2	3.8
Sigmoid colon, Rectum	1	1.9
Total	52.0	100.0

The most common location for neoplasms was the rectum, found in 26.9% of cases. Neoplasms at the recto-sigmoid junction were identified in 19.2%, and those in the ascending colon in 13.5%. Lesions spanning the recto-sigmoid junction and sigmoid colon were observed in 11.5% of cases. Neoplasms involving both the ascending colon and caecum accounted for 9.6%, while those solely in the sigmoid

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

colon were found in 5.8%. The transverse colon was the site in 7.7% of cases, and the descending colon in 3.8%. The combination of the sigmoid colon and rectum hosted a neoplasm in 1.9% of the instances.

Table 5: Type of Growth (n=52)

Type of Growth	Frequency	Percentage
Ulceroproliferative	17	32.7
Circumferential constricting	10	19.2
Ulcero-invasive	9	17.3
Polyp	6	11.5
Constrictive Ulceroproliferative	3	5.8
Annular Fungating	3	5.8
Annular Ulceroproliferative	1	1.9
Constrictive	1	1.9
Proliferative	1	1.9
Proliferative Polypoidal	1	1.9
Total	52.0	100.0

The most frequent type of growth observed was ulceroproliferative, occurring in 32.7% of cases. Circumferential constricting growths were present in 19.2%, followed by ulcero-invasive types in 17.3%. Polyps were identified in 11.5% of the cases. Both constrictive ulceroproliferative and annular fungating types were observed in 5.8% of cases each. The remaining types—annular ulceroproliferative, constrictive, proliferative, and proliferative polypoidal—each constituted 1.9% of the growths.

Table 6: Pathological Risk Factors in the Study Population (n = 52)

Pathological Parameter	Status	Frequency	Percentage (%)
Macroscopic Tumor Perforation	Present	10	19.2
	Not identified	20	38.5
	Not applicable	22	42.3
Lymphovascular Invasion (LVI)	Present	18	34.6
	Not identified	12	23.1
	Not applicable	22	42.3
Perineural Invasion (PNI)	Present	27	51.9
	Not identified	3	5.8
	Not applicable	22	42.3
Resection Margin Status	Free	20	38.5
	Serosal margin involved	5	9.6
	Circumferential resection margin (CRM) involved	3	5.8
	Other margins involved	2	3.8
	Not applicable	22	42.3

Macroscopic tumor perforation was identified in 19.2% of cases, while lymphovascular invasion was present in 34.6% of the study population. Perineural invasion was observed in more than half of the cases (51.9%), indicating aggressive tumor behavior. Resection margins were free of tumor in 38.5% of cases; however, margin involvement, including serosal and circumferential resection margins, was noted in a subset of patients. In 42.3% of cases, these pathological parameters were not applicable, corresponding to non-resection specimens.

Table 7: Frequency of Regional Lymph Node Metastasis in the Study Population

Regional Lymph Node Metastasis	Frequency	Percentage
0 out of 1	4	7.7
0 out of 2	3	5.8
0 out of 3	5	9.6
0 out of 4	4	7.7
1 out of 4	6	11.5
2 out of 10	1	1.9
3 out of 10	1	1.9
3 out of 8	5	9.6
4 out of 10	1	1.9
Not applicable	22	42.3
Total	52	100.0

In the study population of 52 individuals, the frequency of regional lymph node metastasis varied. No metastases were found in 4 participants with 1 node examined (7.7%), in 3 participants with 2 nodes examined (5.8%), in 5 participants with 3 nodes examined (9.6%), and in 4 participants with 4 nodes examined (7.7%). Metastasis in 1 out of 4 nodes was observed in 6 participants (11.5%). Additionally, metastases in 2 out of 10 nodes were found in 1 participant (1.9%), in 3 out of 10 nodes in another

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

participant (1.9%), and in 3 out of 8 nodes in 5 participants (9.6%). Metastasis in 4 out of 10 nodes was noted in 1 participant (1.9%). Data were not applicable (NA) for 22 participants, making up 42.3% of the total.

Table 8: Histopathological Diagnoses (n=52)

Histopathological Diagnoses	Frequency	Percentage
Moderately differentiated Adenocarcinoma	37	71.2
Intramucosal carcinoma	4	7.6
Well differentiated adenocarcinoma	5	9.6
Poorly cohesive carcinoma (signet ring cell type)	1	1.9
Tubular adenoma	3	5.8
Tubular adenoma with high grade dysplasia	1	1.9
Tubulovillous adenoma with high grade dysplasia	1	1.9
Total	52	100.0

In the study group of 52 individuals, the majority of cases, 71.2%, were diagnosed with moderately differentiated adenocarcinoma, making it the most common histopathological diagnosis. Intramucosal carcinoma was observed in 4 cases, accounting for 7.6%. Well-differentiated adenocarcinoma was identified in 5 cases, representing 9.6% of the total. A single case (1.9%) of poorly cohesive carcinoma, specifically of the signet ring cell type, was recorded. Tubular adenomas were found in 3 cases, making up 5.8% of the diagnoses, while tubular adenoma with high-grade dysplasia and tubulovillous adenoma with high-grade dysplasia each appeared in 1 case, both accounting for 1.9% each.

Figure 1: Moderately Differentiated Adenocarcinoma (resected specimen)

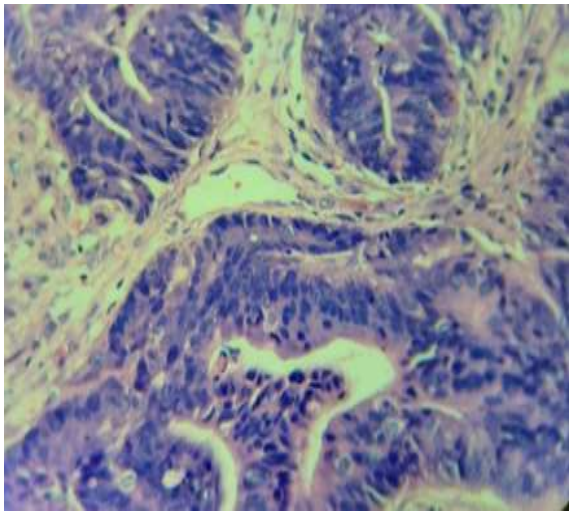

Figure 2: Moderately Differentiated Adenocarcinoma (H&E x400)

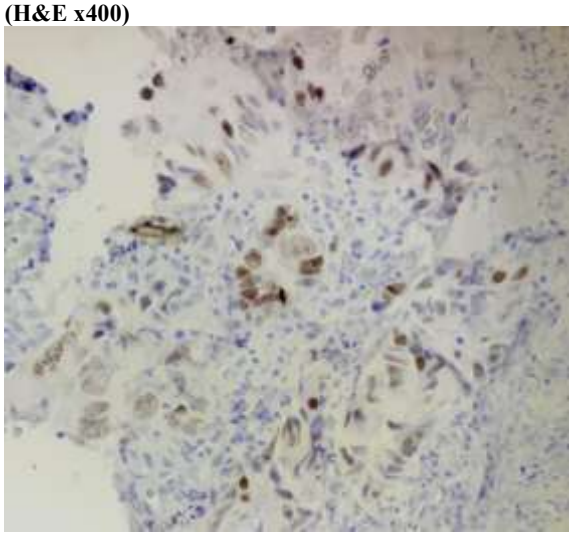

Figure 3: Moderate expression Ki67

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

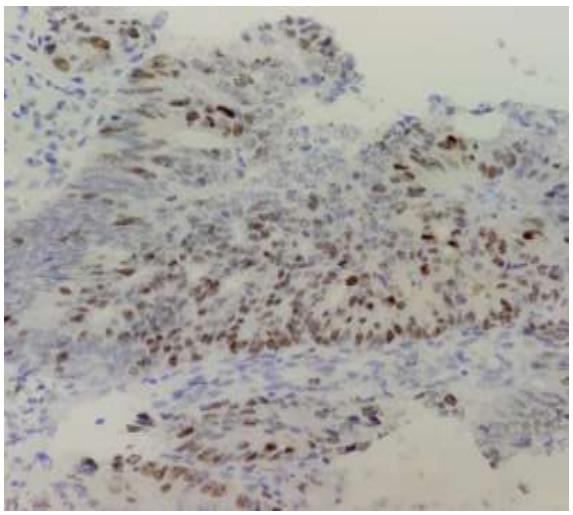

Figure 4: Very Strong expression Ki67

Table 9: Classification of Tumors as Benign or Malignant (n=52)

Classification of Tumors	Frequency	Percentage
Benign	5	9.6
Malignant	47	90.4
Total	52	100.0

The classification of tumors showed that 47 cases (90.4%) were malignant, while 5 cases (9.6%) were benign.

Table 10: Distribution of pTNM Stages

pTNM Stages	Frequency	Percentage
p T3 N0 Mx	**11**	21.2
p T3 N1a Mx	**6**	11.5
p T3 N1b Mx	**3**	5.8
p T4a N0 Mx	**5**	9.6
p T4a N1 Mx	**5**	9.6
NA	**22**	42.3
Total	**52**	100.0

In the study population, the distribution of pTNM stages was as follows: The stage p T3 N0 Mx was the most prevalent, recorded in 11 cases (21.2%). Stages p T4a N0 Mx and p T4a N1 Mx each accounted for 5 cases (9.6%). The p T3 N1a Mx stage was noted in 6 cases (11.5%), and p T3 N1b Mx was seen in 3 cases (5.8%). Data were not applicable (NA) for 22 cases, making up 42.3% of the total.

Table 11: IHC grading & staging (Ki67 expression)

IHC Grading	IHC Staging	Frequency	Percentage
Mild expression	1+	19	36.6
Moderate expression	2+	15	28.8
Strong expression	3+	4	7.7
Very Strong	4+	2	3.8
N/A	0	12	23.1
Total		52	100.0

In the study population of 52 individuals, the distribution of Ki67 expression based on immunohistochemistry (IHC) grading and staging showed mild expression (1+) in 19 cases (36.6%), moderate expression (2+) in 15 cases (28.8%), and strong expression (3+) in 4 cases (7.7%). Very strong expression (4+) was observed in 2 cases (3.8%). Data were not applicable(N/A) for 12 cases, which constitutes 23.1% of the total.

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

Table 12: Histopathological Grading and Staging

Histopathology	HP Grade	HP staging
Benign	NA (n=5)	NA-(5)
Intramucosal carcinoma	Grade – 0 (n=4)	NA- (4)
Well differentiated	Grade – 1 (n=5)	NA=(2)
		II A=(3)
Moderately differentiated	Grade – 2 (n=37)	NA =(10)
		II A=(8)
		II B=(5)
		III B =(14)
Poorly differentiated	Grade – 3 (1)	Negative =(1)
Total	52	52

Histopathology findings revealed 52 cases categorized by HP grade and staging as follows: Benign: 5 cases, HP Grade NA, Staging NA. Intramucosal carcinoma: 4 cases, Grade 0, Staging NA. Well-differentiated carcinoma: 5 cases, Grade 1, staged as NA (2) and IIA (3). Moderately differentiated carcinoma: 37 cases, Grade 2, with staging distributed as NA (10), IIA (8), IIB (5), and IIIB (14). Poorly differentiated carcinoma: 1 case, Grade 3, Staging Negative (1).

Table 13: IHC (Ki67 expression)

Percentage	Frequency	Grade	IHC Expression	Stage
0 - 20	12	1+	No expression	Negative
21 – 40	19	2+	Mild expression	Mild positive
41 – 60	15	3+	Moderate expression	Moderate positive
61 – 80	04	3+	Strong expression	Strong positive
81 - 100	02	4+	Very strong positive	Very strong positive

The immunohistochemical (IHC) expression and staging across different percentage ranges as follows: 0-20%: 12 cases, Grade 1+, No expression, Stage Negative.
21-40%: 19 cases, Grade 2+, Mild expression, Stage Mild positive.
41-60%: 15 cases, Grade 3+, Moderate expression, Stage Moderate positive.
61-80%: 4 cases, Grade 3+, Strong expression, Stage Strong positive.
81-100%: 2 cases, Grade 4+, Very strong expression, Stage Very strong positive.

DISCUSSION

The present study evaluated the clinicopathological characteristics of colorectal neoplasms with special emphasis on Ki-67 immunohistochemical expression and its correlation with histopathological grade and tumor stage. The mean age of patients in the present series was 57.03 ± 11.33 years, with a peak incidence in the fifth and sixth decades. Similar age distributions have been reported by Sung et al,[1] and Arnold et al,[7] who observed that colorectal cancer incidence increases significantly after 50 years of age, particularly in developing countries. The male predominance observed in our study (male-to-female ratio 2.5:1) is comparable to findings by Gupta et al,[8] and Norat et al,[9] who attributed this trend to lifestyle and dietary risk factors.
Clinically, altered bowel habits and abdominal pain were the most frequent presenting complaints, followed by rectal bleeding and weight loss. These findings are in agreement with studies by Lee et al,[10] and Benson et al,[11] who reported that nonspecific gastrointestinal symptoms often lead to delayed diagnosis and advanced disease at presentation. The high prevalence of non-vegetarian diet, smoking, and alcohol consumption in our cohort further supports established epidemiological associations with colorectal carcinogenesis.
Histopathologically, adenocarcinoma constituted the majority of cases, with moderately differentiated adenocarcinoma being the most common subtype. This observation is consistent with reports by Washington et al,[12] and Risio,[13] who documented similar distributions of histological grades. The rectum and rectosigmoid junction were the most frequently involved sites, which aligns with Indian and Asian studies reporting a predominance of distal colorectal cancers.[8,11]
Adverse pathological features such as lymphovascular invasion, perineural invasion, and tumor perforation were frequently observed in the present study, indicating aggressive tumor behavior. Liebig et al,[14] and Huh et al,[15] have demonstrated that perineural invasion and lymphovascular invasion are independent predictors of poor prognosis and advanced tumor stage in colorectal cancer.
Immunohistochemical analysis revealed increasing Ki-67 expression with higher histological grade and advanced pTNM stage. These findings are concordant with studies by Yan et al,[16] and Vogt et al,[17] who reported a significant association between high Ki-67 labeling index and aggressive tumor characteristics, including nodal metastasis and advanced stage. Conversely, Melling et al,[18] and Fluge et al,[19] reported that high Ki-67 expression was associated with favorable survival, particularly in patients receiving adjuvant chemotherapy. The discrepancy may be explained by differences in patient populations, treatment status, and Ki-67 cut-off values. Since survival analysis was not included in the present study, Ki-67 expression primarily

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

reflected tumor proliferative activity rather than treatment response.

Overall, the present findings support the role of Ki-67 as a useful adjunct marker of tumor proliferation and biological aggressiveness in colorectal adenocarcinoma when interpreted alongside conventional histopathological parameters.

CONCLUSION

The present study highlights the clinicopathological spectrum of colorectal neoplasms and demonstrates the relevance of Ki-67 as an immunohistochemical marker of tumor proliferative activity. Colorectal adenocarcinoma was the predominant histopathological diagnosis, with a higher frequency observed in the fifth and sixth decades of life and a marked male predominance. Adverse pathological features such as lymphovascular invasion, perineural invasion, and advanced tumor stage were frequently encountered, indicating aggressive tumor behavior.

A progressive increase in Ki-67 expression was observed with higher histopathological grade and advanced pTNM stage, suggesting a strong association between tumor proliferative activity and biological aggressiveness. These findings support the role of Ki-67 as a useful adjunct to conventional histopathological parameters in assessing tumor behavior and risk stratification in colorectal adenocarcinoma.

Although Ki-67 should not be used as an isolated prognostic marker, its interpretation alongside established clinicopathological factors may aid in identifying patients with biologically aggressive disease who may benefit from closer surveillance and individualized therapeutic strategies. Further large-scale, multicentric studies incorporating survival outcomes are warranted to validate the prognostic and predictive utility of Ki-67 in colorectal cancer.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide. CA Cancer J Clin. 2021;71(3):209–249.
2. Weiser MR. AJCC 8th edition: colorectal cancer. Ann Surg Oncol. 2018;25(6):1454–1455.
3. Scholzen T, Gerdes J. The Ki-67 protein: from the known and the unknown. J Cell Physiol. 2000;182(3):311–322.
4. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2011;144(5):646–674.
5. Jahan SI, et al. Association of Ki-67 proliferation index with grade and stage of colorectal carcinoma. J Pathol Transl Med. 2020;54(5):394–401.
6. Melling N, et al. High Ki-67 expression is associated with improved survival in colorectal cancer. Br J Cancer. 2016;115(5):541–548.
7. Arnold M, Sierra MS, Laversanne M, et al. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683–691.
8. Gupta S, Bhattacharya D, Acharya AN, et al. Colorectal cancer in India: emerging trends and risk factors. Indian J Cancer. 2022;59(1):1–6.
9. Norat T, Lukanova A, Ferrari P, Riboli E. Meat consumption and colorectal cancer risk. Int J Cancer. 2002;98(2):241–256.
10. Lee YM, Law WL, Chu KW, Poon RT. Emergency surgery for obstructing colorectal cancers. J Am Coll Surg. 2001;192(6):719–725.
11. Benson AB, Venook AP, Al-Hawary MM, et al. NCCN guidelines insights: colon cancer. J Natl Compr Canc Netw. 2018;16(4):359–369.
12. Washington MK, Berlin J, Branton P, et al. Protocol for examination of colorectal carcinoma specimens. Arch Pathol Lab Med. 2009;133(10):1539–1551.
13. Risio M. The natural history of adenomas. Best Pract Res Clin Gastroenterol. 2010;24(4):397–406.
14. Liebig C, Ayala G, Wilks J, et al. Perineural invasion is an independent predictor of outcome in colorectal cancer. J Clin Oncol. 2009;27(31):5131–5137.
15. Huh JW, Kim HR, Kim YJ. Prognostic significance of perineural invasion in colorectal cancer. Ann Surg Oncol. 2010;17(8):2066–2072.
16. Yan MY, Wang YX, Zhu JQ, et al. Prognostic significance of Ki-67 expression in colorectal cancer. World J Gastroenterol. 2010;16(41):5172–5177.
17. Vogt A, et al. Ki-67 expression and survival in colorectal cancer. Oncol Lett. 2013;6(6):1507–1512.
18. Melling N, et al. High Ki-67 expression is associated with improved survival in colorectal cancer. Br J Cancer. 2016;115(5):541–548.
19. Fluge Ø, et al. Prognostic relevance of Ki-67 in colorectal cancer. J Clin Pathol. 2009;62(7):571–575.

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