Original Research Paper

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Histopathology

EVALUATE THE IMMUNOHISTOCHEMICAL EXPRESSION OF Ki67 IN BENIGN, PREMALIGNANT AND MALIGNANT LESIONS OF COLON AND RECTUM.

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ABSTRACT **Introduction:** Colorectal carcinoma is the third most common cancer worldwide, accounting for approximately 10% of all cancer cases. Both cellular proliferation and oncogenesis depend on to maintain tissue homeostasis. Tumour aggressiveness can be determined by measuring the proliferation index of the Ki67. **Objectives:** Evaluate and compare the immunohistochemical expression of Ki67 in benign, premalignant and malignant lesions of colon and rectum and to assess the Ki67 over expression in different age groups and various tumour types. **Methods:** In this cross-sectional study, the archives of pathology reports of colon and rectal biopsies and resected specimens over the time period of 1 ½ years (from September, 2022 to March, 2024) were collected from the histopathology records. Immunohistochemistry (IHC) was applied to all the paraffin fixed tissue blocks having area of interest. Finally, Ki67 expression was calculated by light microscopy. **Results:** Study included benign, premalignant, and malignant lesions of colon and rectum where Ki67 is highest in malignant followed by premalignant and benign lesions with mean Ki67 is 74.16%, 64.84%, and 23.98% respectively. The mean age of 46 years, male to female ratio 1.5:1 and rectal lesions are more common than colon lesions. Tubulovillous adenoma has more Ki67 index as compared to tubular adenoma. Ki67 index is more in high grade dysplasia as compared to low grade dysplasia, similarly Ki67 index is more in well differentiated as compared to moderate and poorly differentiated adenocarcinoma. Statistically insignificant relation between clinicopathological findings (i.e., age, gender and location of lesions) and Ki67 proliferation index is noted. **Conclusion:** Thus, Ki67 proliferation index can't be used alone for calculating the prognosis in colorectal lesions as it was not significantly related to clinicopathological variables.

KEYWORDS : Colorectal lesions; Ki67 index; Immunohistochemistry.

INTRODUCTION

Cancer that originates from the caecum to the anus is referred to as colorectal cancer (CRC). Colon cancer, which extends from the caecum to the rectosigmoid colon (nearly 15 cm above the anal canal margin), and rectal cancer, which extends from the rectosigmoid colon to the anal canal, are the two subtypes of colorectal carcinomas. It initiates as a benign polypoidal growth over the colon's or rectum's inner lining and develops gradually over ten to twenty years[1,2].

Multistage genetic mutations are associated with the genesis and evolution of adenomatous polyps into cancer, which are regarded as lesions with malignant potential[3,4]. Prominent villous component, high degree of atypia, and large size are known histopathological variables that increase the risk for malignant transformation[5].However, investigation of genetic instability during the advancement of adenoma-carcinoma has shown several processes that modify the regulation of cell proliferation and death, and a variety of oncogenic traits have been explored as putative risk factors linked to the development of malignancy[6-8]. Patients with ulcerative colitis have a long-term risk of CRC[9].An unhealthy lifestyle, which includes obesity, sedentary behaviour, a diet high in meat, calories, and fat but low in fiber, excessive alcohol intake, and smoking, increases the risk of colon cancer[10-12]. The development of CRC is more common in people with genetic syndromes such as Lynch Syndrome (HNPCC) and Familial Adenomatous Polyposis (FAP)[13].

With the exception of phase G0, all histonic cycle phases contain the non-histonic protein nuclear antigen Ki67, which is essential for cell proliferation[14]. Ki67 index is well-known for determining the prognosis, e.g., breast cancer, gastrointestinal cancer, and prostate cancer, in the majority of studies that used immunohistochemical markers[15-18].Using the Ki67 monoclonal antibody to assess colorectal polyps, changes in their cell kinetics have been linked to a few histological risk markers for cancer[6] .Both cellular proliferation and oncogenesis depend on each other to maintain tissue homeostasis. Tumour aggressiveness can be determined by measuring the proliferation index of the Ki67 protein (pKi67), which is linked to intrinsic cell populations' proliferation in malignant tumours. Thus, Ki67 IHC staining can be used to determine the prognosis for a variety of tumour types and subtypes. Also, by using the proliferation index of Ki67, treatment protocols can be planned accordingly.

According to WHO July, 2023 factsheets, "CRC is the third most common cancer worldwide, accounting for approximately 10% of all cancer cases, and is the second leading cause of cancer-related deaths worldwide. By the year 2040, CRC cases will increase to 3.2 million new cases per year (an increase of 63%) and 1.6 million deaths per year (a rise of 73%[19]."

Aim And Objectives

Aim-

Evaluate the immunohistochemical expression of Ki67 in benign, premalignant and malignant lesions of colon and rectum.

Objectives-

1) To evaluate and compare the expression of Ki67 in benign lesions, premalignant lesions and malignant colorectal lesions.
2) To assess the Ki67 over expression in different age groups and various tumour types.

MATERIALS AND METHODS

Study Design: It is a cross-sectional study.

Sample Selection:

I. Inclusion Criteria

1) Histopathologically confirmed cases of benign, premalignant, and malignant colorectal lesions.
2) The tissue should be adequate for further processing of Ki67 IHC.
3) Clinical details should be present for correlation.

ii. Exclusion criteria

1) Inadequate and autolyzed tissue.
2) Neoadjuvant chemotherapy and/or radiotherapy treated the patient's colonoscopic biopsy or resected colorectal specimens.

Sampling

Post surgical specimens, including colonoscopic biopsies and resected colorectal specimens, were collected. The gross examination of all specimens, were performed and sections were taken from representative areas. Blocks were prepared in paraffin wax with the help of a paraffin embedding station. These tissue blocks received from biopsy samples and resected colorectal specimens, which were diagnosed by histopathological examination on H&E-stained, were then used for evaluation of the Ki67 expression, and the Ki67 index was calculated. A total 120 cases were included in our study. Relevant demographic and clinicopathological data like age, sex, site of lesion, and other essential information were noted from the archives of the histopathological record.

Methodology

The H&E-stained sections are made from tissue blocks of all the cases of colon and rectal lesions collected from the pathology department of S.N. Medical College and Hospital over a period of 1 ½ years (from September, 2022 to March, 2024). Their respective tissue sections were also obtained. Then H&E-stained slides that contained complete sections were examined for the areas of well stained tumour cells. The corresponding tissue blocks were also collected. The thickness of tissue sections was maintained at 3-4 µm and transferred to the APES (3-aminopropyltriethoxysilane) coated slide surface. Following this, incubation of slides was done between 58^{0}C to 60^{0}C for 30 minutes to1 hour. In our institution, antigen retrieval was done by the Multi Epitope Retrieval System (MERS) which produces even heating. It causes fewer disadvantages as compared to other methods. A 3-4 µ thick sections of tissue samples were then transferred onto the coated slides. MERS based heat induced antigen retrieval was used. The specific antigen binds with rabbit monoclonal antibody Ki67 and is then identified by adding the 2^{0}antibody conjugated with HRP- polymer and di-amino-benzidine substrate. Antigen species (clone) dilution control slide was used. Steps for IHC were followed as given by the manufacturer (by Path n Situ).

Immunohistochemical Evaluation And Ki67 Calculation

For calculation, the staining results were categorized into 3 categories (low, intermediate, and high) according to the percentage of cells with nuclear positivity of Ki67 stain in malignant cells, as follows: low Ki67 (0%–10%); intermediate Ki67 (>10% and up to 25%); high Ki67 (25% and more)[15].

Ethical Considerations

The study was conducted only after being approved by the Institutional Ethical Committee (IEC) of Sarojini Naidu Medical College and Hospital, Agra.

Plan For Data Analysis

The data for the present study was entered in Microsoft Excel 2019 and analyzed using SPSS statistical software 23.0 Version. The descriptive statistics included frequency and percentage. Mean and standard deviation. The level of significance for the present study was fixed at 5%.

The ordinal and nominal variables were compared using the Chi Square test. The intergroup comparison was done using independent t tests and the one-way ANOVA test. The Shapiro–Wilk test was used to investigate the distribution of the data and Levene's test to explore the homogeneity of the variables.

OBSERVATIONS AND RESULTS

Analysis Of Data By Statistical Tools

The archives of data were collected, and the statistical relationship between the colorectal lesions and clinicopathologic variables was analyzed. Chi –square test was used for the analysis. The probability factor (p-value) was calculated for the assessment of the significance of observations. Observations were considered statistically significant whenever the p-value was come out to be less than <0.05 or <0.001.

Of the 120 cases included in the study, the majority of the patients were between 51 years to 70 years old, which constituted 39% of the total cases. The patient's age ranges from 6 months to 83 years, with a **mean age of 46 years**. The male-to-female ratio was **1.5:1**. The right colon lesion constitutes 32.5%, the left colon lesion constitutes 34.1%, and the rectal lesion constitutes 33.4% of the cases and 35% were benign, 16% were premalignant, and malignant comprised of 49% of the cases.

Table 1: Distribution Of Colorectal Lesions Based On Histopathological Type

Histologic type	Number of cases	Percentage %
Benign lesions (n=42)		
Non-specific inflammation	23	19.16%
Inflammatory bowel disease	06	5%
Tubercular inflammation	05	4.16%
Hirschsprung's disease	03	2.5%
Juvenile polyp	05	4.16%
Benign tumours and premalignant lesions (n=19)		
Tubular adenoma with low grade dysplasia	08	6.67%
Tubular adenoma with high grade dysplasia	09	7.5%
Tubulo-villous adenoma with low grade dysplasia	01	0.83%
Tubulo-villous adenoma with high grade dysplasia	01	0.83%
Malignant lesions (n=59)		
Adenocarcinoma, NOS	48	40.00%
Mucinous adenocarcinoma	03	2.50%
Adenocarcinoma with mucinous component	01	0.83%
Signet ring cell carcinoma	03	2.50%
Mucinous adenocarcinoma with Signet ring cell carcinoma component	01	0.83%
Basoloid SCC	01	0.83%
Neuroendocrine tumour	02	1.67%
Total	**120**	**100%**

Of the 120 patients analyzed, the most common lesions in the benign category were non-specific inflammation, constituting 19.16% of the cases, followed by inflammatory bowel disease (5%), tubercular inflammation (4.16%), juvenile polyp (4.16%), and hirschsprung's disease (2.5%). Among premalignant lesions, tubular adenoma with high grade dysplasia was the most common, constituting 7.5% of the cases, followed by tubular adenoma with low grade dysplasia (6.67%), tubulovillous adenoma with high grade (0.83%), and tubulo-villous adenoma with low grade dysplasia (0.83%). In the malignant category, the most common lesion was adenocarcinoma, NOS which constitutes 40% of all cases, followed by mucinous adenocarcinoma (2.5%), signet ring cell carcinoma (2.5%), and neuroendocrine tumour (1.67%). Among the total of 19 premalignant lesions, 47.4% (n=9) of the cases were of low-grade dysplasia and 52.6% (n=10) were of high-grade dysplasia. Out of 55 malignant cases, well differentiated cases were 35.4%, followed by moderately differentiated cases at 41.6%, and poorly differentiated cases 23%.

Table 2: Correlation Between Histologic Categories Of Lesions And Ki67 Index

Category of lesions	No of cases	Mean Ki67 index	S.D.	P value
Benign	42	18.33%	18.877	0.001 (sig.)
Premalignant	19	64.84%	17.917	
Malignant	59	74.16%	11.477	

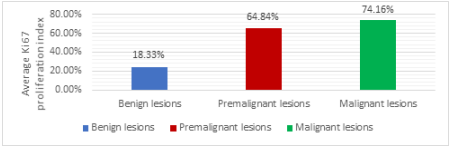

Chart 1: Correlation Between Histologic Categories Of Lesions And Ki67 Index.

In our study, benign lesions showed a mean Ki67 value of 18.33%, followed by premalignant lesions with a mean value of 64.84% and malignant lesions with a mean value of 74.16%. The relationship between the histologic category of lesions and Ki67 was highly statistically significant (p value less than 0.001) when assessed by the ANOVA test.

Table 3: Correlation Between Histologic Categories Of Lesions And Different Ki67 Proliferative Index Category

Category of lesions	Low	Intermediate	High	Chi Square	P value
Benign (42)	31	0	11	82.358	0.0001 (Sig.)
	73.8%	0%	26.2%		

Premalignant (19)	0	1	18		
	0%	5.3%	94.7%		
Malignant (59)	0	0	59		
	0%	0%	100.0%		

In our study, 100% of malignant cases showed high proliferative activity. In premalignant lesions, high proliferative activity was shown by 94.7% of cases, and intermediate proliferative activity was shown by 5.3%. In benign lesions, 73.8% cases showed low proliferative activity, and 26.2% of cases had high proliferative activity. The relationship among histologic categories and Ki67 proliferative index was statistically highly significant (probability value <0.001), calculated by the Chi square test.

Table 4: Correlation Of Histological Subtype Of Colorectal Lesions With Ki67 Index

Histological category	Cases	Mean Ki67	S.D.	S.E.	P value
Non-specific inflammation	23	8.695	0.470	0.098	**0.001 (Sig)**
Inflammatory bowel disease	6	54.166	12.812	5.230	
Tubercular inflammation	5	8.400	0.547	0.244	
Hirschsprung's disease	3	8.666	0.577	0.333	
Juvenile polyp	5	40.000	9.055	4.049	
Tubular adenoma	17	63.764	18.478	4.481	**0.001 (Sig)**
Tubulo-villous adenoma	2	74.000	11.313	8.000	
Adenocarcinoma, NOS	48	75.833	10.081	1.455	**0.001 (Sig)**
Mucinous adenocarcinoma	3	67.333	9.291	5.364	
Adenocarcinoma with mucinous component	1	60.000	.	.	
Signet ring cell carcinoma	3	57.000	9.643	5.567	
Mucinous adenocarcinoma with Signet ring cell carcinoma component	1	60.000	.	.	
Basoloid SCC	1	90.000	.	.	
Neuroendocrine tumour	2	76.500	26.162	18.500	

In this study, the correlation between histological subtype and Ki67 index was statistically highly significant (p value- <0.001) by applying the ANOVA test. In benign lesions, inflammatory bowel disease has the highest mean Ki67 index is of inflammatory bowel disease (54.16%), followed by juvenile polyps (40%). Among premalignant lesions, the highest Ki67 is seen in tubulovillous adenoma (74%) followed by tubular adenomas (63.764%). In malignant lesions, non-mucinous adenocarcinoma (adenocarcinoma, NOS), has a higher mean Ki67 index (75.83) than mucinous adenocarcinoma (67.33%) and signet ring cell adenocarcinoma (57%). The highest mean Ki67 index is observed in basaloid squamous cell carcinoma (90%), followed by neuroendocrine tumour (76.5%).

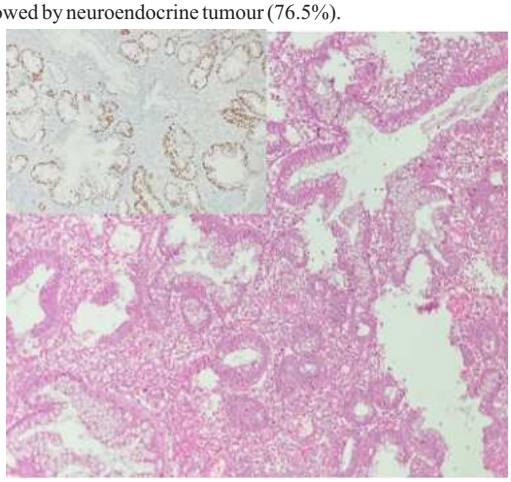

Figure 1: Microscopic picture of juvenile polyp. H& E stain. Objective 10X. Section examination shows edematous lamina propria with inflammatory cells and cystically dilated glands filled with mucus and inspissated inflammatory debris. Inset shows Ki67 immunostaining in juvenile polyp. Ki67 index is 40%.

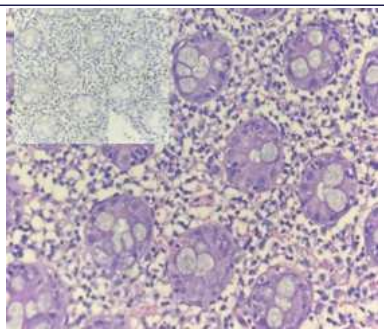

Figure 2: Microscopic picture of non-specific inflammation. H&E stain. Objective 40X. Section examination showing focal inflammation in the mucosa. Inset shows Ki67 <2%.

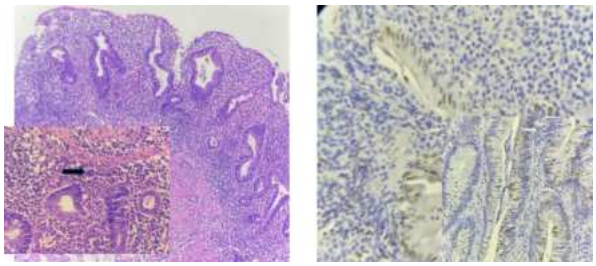

Figure 3: Microscopic picture of inflammatory bowel disease. H&E stain. Objective 10X. Section shows widely spaced glands, crypt architectural distortion, cryptitis, crypt abscess, diffuse active inflammation of lamina propria, erosion and ulceration of mucosa. Inset shows basal plasmacytosis in lamina propria. Arrow shows plasma cell.

Figure 4: Microscopic picture of Ki67 immunostaining of inflammatory bowel disease. Objective 40X. Shows Ki67 index is 30%.

Table 5: Correlation Between Histologic Grade Of Dysplasia Of Premalignant Lesions And Ki67 Index Using Independent T Test

Dysplasia	CASES	Mean Ki67 index	S.D.	Std Error	T value	P value
Low	09	56.33	19.874	6.624	4.635	0.001
High	10	72.50	12.385	3.916		

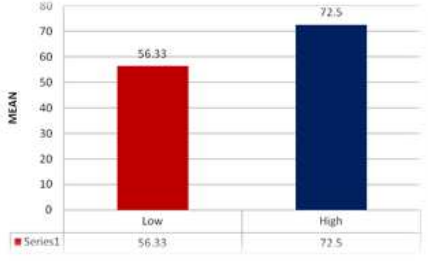

Chart 2: Correlation Between Histologic Grade Of Dysplasia Of Premalignant Lesions And Ki67 Index Using Independent T Test

The correlation between the histological grade and Ki67 index was statistically significant when analyzed using an independent t test, with higher values in subjects with high grade dysplasia (72.50%) as compared to low grade dysplasia (56.33%).

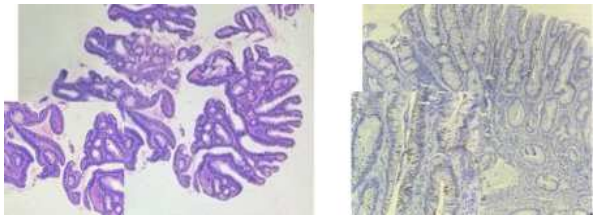

Figure 5: Microscopic picture of tubular adenoma with low grade dysplasia. H&E stain. Objective 4X. Section examined shows complex pattern of glands including cribriforming. Apical mucin is lost and nuclei show complete loss of polarity. Inset shows dysplastic nuclei extending upto the cell surface. Mitosis is also present.

Figure 6: Microscopic picture of immunostaining Ki67 of tubular adenoma with low grade dysplasia. Objective 10X. Inset shows Ki67 index is 30%.

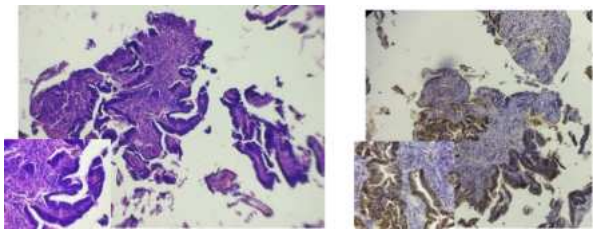

Figure 7: Microscopic picture of tubular adenoma with high grade dysplasia. H&E stain. Objective 10X. Section examined shows glands having variability and architectural complexity along with back-to-back crypt formation. Inset shows nuclear polarity is lost.

Figure 8: Microscopic picture of immunostaining Ki67 of tubular adenoma with high grade dysplasia. Objective 10X. Inset shows Ki67 index 75%.

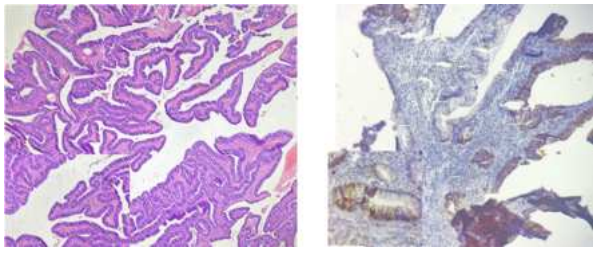

Figure 9: Microscopic picture of tubulovillous adenoma with high grade dysplasia. H&E stain. Objective 4X. Section examined shows complex branching tubules and villous component. Inset shows elongated and dysplastic nuclei extending upto the cell surface.

Figure 10: Microscopic picture of immunostaining Ki67 of tubulovillous adenoma with low grade dysplasia. Objective 10X. Ki67 index is 60%.

Table 6: Correlation Between Histologic Differentiattion Of Malignant Lesions And Ki67 Index

Differentiation	Cases	Mean	S.D.	F value	P value
Well	19	85.88	11.645	30.658	0.001 (Sig)
Moderate	22	73.45	4.962		
Poor	14	64.63	4.467		

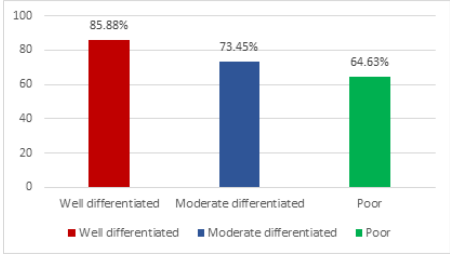

Chart 3: Correlation Between Histologic Differentiation Of Malignant Lesions And Ki67 Index

In our study, well differentiated tumours showed a mean Ki67 value of 85.88%, followed by moderately differentiated tumours with a mean value of 73.45% and poorly differentiated tumours with a mean value of 64.63%. The relationship between histologic differentiation and Ki67 was highly statistically significant (p value less than 0.001) when assessed by the ANOVA test.

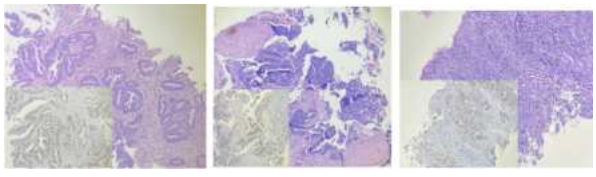

Figure 11: Microscopic picture of well differentiated adenocarcinoma. H& E stain. Objective 4X. Section examined shows well-formed glands invading the muscularis mucosa. Inset shows Ki67 index is 85%.

Figure 12: Microscopic picture of moderately differentiated adenocarcinoma showing readily identifiable glands. H&E stain. Objective 10X. Inset shows Ki67 index 70%.

Figure 13: Microscopic picture of poorly differentiated adenocarcinoma. H&E stain. Objective 10X. Section examined shows tumour cells in solid sheets with minimal or no gland formation. Inset shows Ki67 index 65%.

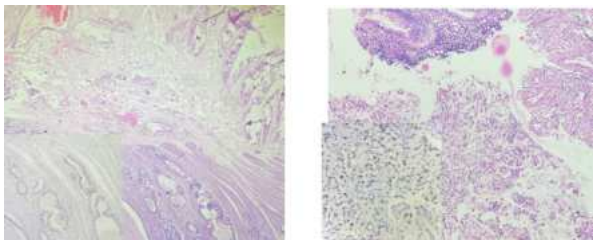

Figure 14: Microscopic picture of mucinous adenocarcinoma. H&E stain. Objective 4X. Section examined shows lesion composed of extracellular mucin that contain overt malignant epithelium cells as clumps, layers and signet ring cells. Inset shows Ki67 index 70%.

Figure 15: Microscopic picture of signet ring cell adenocarcinoma. H&E stain. Objective 10X. Section examined shows cytologically disrupted malignant cells by intracellular mucin, displacing the nucleus to the periphery of the cells. Inset shows Ki67 index 50%.

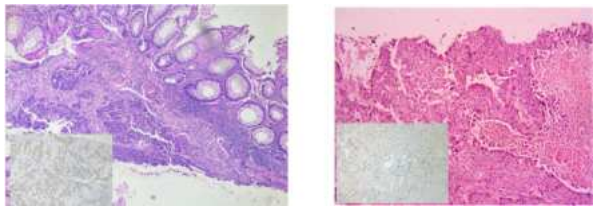

Figure 16: Microscopic picture of basaloid squamous cell carcinoma. H& E stain. Objective 10X. Section examined shows subepithelial basaloid neoplasm with microcystic nests, strands, trabeculae of tumor cells infiltrating a myxoid stroma. Inset shows Ki67 index 90%.

Figure 17: Microscopic picture of neuroendocrine tumour. H& E stain. Objective 10X. Section examined shows tumor cells arranged in nests and insular pattern, monotonous regular cells with round or oval nuclei with salt and pepper chromatin and moderate eosinophilic granular cytoplasm. Inset shows Ki67 index is 95%.

Table 7: Correlation Between Ki67 Index And Clinicopathological Variables

Clinicopathological parameters		Total	Low Ki67	Intermediate Ki67	High Ki67	P-value by Chi-square
Age group of cases	<30 years	27	4	0	23	Chi Sq-9.747 P value - 0.057 (NS)
		22.5%	14.82%	.0%	85.18%	
	30-50 years	31	11	0	20	
		25.8%	35.5%	.0%	64.5%	
	>=50years	62	16	1	45	
		51.7%	25.80%	1.6%	72.58%	
Gender	Female	47	11	0	36	Chi sq-0.932 P value - 0.637 (NS)
		39%	23.4%	.0%	76.6%	
	Male	73	20	1	52	
		61%	27.4%	1.4%	71.2%	
Site	Right colon	39	8	0	31	Chi sq-9.013 P value - 0.063 (NS)
		33%	20.5%	.0%	79.5%	
	Left colon	41	17	0	24	
		34%	41.5%	.0%	58.5%	
	Rectum	40	6	1	33	
		33%	15.0%	2.5%	82.5%	

The correlation between the age groups and proliferative index of Ki67 was statistically non-significant with a probability value (P-value 0.057). 85.18% of the subjects in the age group < 30 years had high scores, whereas 72.58% of the subjects in the >50 years age group had high scores and 51.7% had low scores. The correlation between gender and Ki67 index was statistically non-significant (P-value 0.637), with 76.6% of the females having high Ki67 scores and 71.2% of the males having a high Ki67 index. The correlation between the site and Ki67 index was statistically non-significant (P-value 0.063), with 82.5% of the rectum, 79.5% of the right colon, and 58.5% of the left colon having a high Ki67 index.

DISCUSSION

The prognosis for colorectal cancer varies depending on the stage of diagnosis. Early-stage cancers have higher survival rates than advanced-stage cancers. Early diagnosis, surgery, better knowledge of its clinicopathological prognostic factors, and response to adjuvant therapy have contributed to a better outcome in affected patients[19].

A comparative study between different categories of the colorectal lesions and the Ki67 proliferative index

The present study showed that a statistically significant relationship was noted among the Ki67 index and histological categories of colorectal lesions. The expression of Ki67 was lower in benign lesions, followed by premalignant lesions (adenomas), and highest in malignant colorectal lesions. Lin, M.X., et al[20], study also concluded that the expression of Ki67 was significantly higher in CRC than in adenomas and normal colorectal mucosal tissues. Similar results were concluded by Heidari, Z., et al[21],and Nayak, J., et al[22].

Nayak, J., et al[22], also observed that among non-neoplastic polyps, juvenile polyps have a lower Ki67 index as compared to neoplastic polyps (adenomas). Among benign lesions, inflammatory bowel disease and juvenile polyps have a significantly higher Ki67 index as compared to other benign lesions.

A comparative study of histological subtype with Ki67 proliferation index in colon and rectal carcinoma's

The present study shows that a statistically significant relationship was observed between the Ki67 proliferative index and histological subtypes. Non-mucinous adenocarcinomas have higher Ki67 index as compared to mucinous and signet ring cell adenocarcinomas. The same was reported in several other studies[22-24]. Ahmed, N.Y., et al[24], found that the Ki67 index was high (+31/40) in non-mucinous colorectal lesions as compared to mucinous and signet cell adenocarcinoma (+0/5). On the other hand, Lanza, G. J., et al[25], noticed higher levels of Ki67 index in mucinous than non-mucinous adenocarcinomas. Contrary to the above findings, Melling, N., et al[15], found that the correlation between the histological type of the tumour and Ki67 expression was insignificant.

A comparative study between grade of dysplasia in premalignant colorectal lesions and Ki67 expression

The present study shows a significant correlation between the grade of dysplasia and Ki67. An increased Ki67 index was observed with high grade dysplasia (mean=72.50) as compared to low grade dysplasia (mean=56.33). Similar findings were observed by Nussrat, F.L., et al[26], with a mean Ki67 index of 33.20 for high grade dysplasia as compared to a mean Ki67 index of 13.93 for low grade dysplasia. This study also agrees with the findings of Sjoqvist, U., et al[9], and Suheil, S.S., & Mahdi, L.H[27]. Contrary to the above findings, Sousa, W., et al[28], concluded that the correlation between the grade of dysplasia and the Ki67 index was insignificant.

Comparative study of histologic differentiation in various colorectal carcinoma's and Ki67 index

The present study shows that there was a significant relationship between the Ki67 index and histological grade. The Ki67 index was highest in well differentiated adenocarcinomas if compared with moderate and poorly differentiated adenocarcinoma. Similar observations were noted by Ahmed, N.Y., et al[24], and a review article written by Mulyawan, I.M.[23], studied that the Ki67 proliferative index was lower in poorly differentiated carcinoma as compared to moderately differentiated and well differentiated adenocarcinomas. Melling, N., et al[15], and Dharmayuda, T.G.[29], also concluded that Ki67 positivity was higher in well differentiated adenocarcinomas when compared with moderately differentiated adenocarcinomas followed by poorly differentiated adenocarcinoma. It showed that proliferative activity was lower in tumour with poor differentiation. In contrast to the above findings, studies conducted by LIU, Q.I. et al[30], and Heidari, Z., et al[21], concluded that Ki67 proliferative index was less in well differentiated carcinoma as compared to moderately differentiated and poorly differentiated adenocarcinoma.

A Comparative Study Between Clinicopathologic Variables And Ki67 Index In Various Colorectal Lesions

The present study shows that there was a statistically insignificant relationship between clinicopathological variables and the Ki67 index. Many other studies also state that there was an insignificant relation between the Ki67 proliferation index and clinicopathologic variables such as age, sex, and location of lesions[15,21,24,30,31]. This weak correlation was due to noticeable heterogenicity in colon and rectal cancers[32].

CONCLUSIONS

The IHC test for calculating the Ki67 proliferative index is simple and can be applied over tissue blocks. The present study concluded that, the expression of Ki67 is lower in benign lesions, followed by premalignant lesions (adenomas), and highest in malignant colorectal lesions. Among benign lesions, the Ki67 proliferative index was significantly higher in juvenile polyps and inflammatory bowel disease as compared to other benign lesions. Among premalignant lesions, the Ki67 proliferation index was significantly related to the grade of dysplasia in adenomas of the colorectal region, but the Ki67 proliferative index has an insignificant relationship with the clinicopathological variables. Thus, the Ki67 proliferative index can be used for routine pathological evaluation with consideration of various other parameters in cases of dysplasia in colorectal adenomas. Also, high grade dysplasia with a significant positive Ki67 index could be used as an aid to assess high-risk groups and the formation of novel guidelines for estimation of prognosis and precise management in the clinical scenario.

Colorectal non-mucinous adenocarcinomas with similar (mucinous) and poor prognosis (signet ring cell) express a significantly high Ki67 index, and therefore they may require a different therapeutic approach. Considering the glandular differentiation, well-differentiated adenocarcinomas have a higher Ki67 index as compared to moderately differentiated and poorly differentiated adenocarcinomas.

Hence, the Ki67 proliferation index can't be used alone for calculating the prognosis in CRC as it is not significantly related to clinicopathological variables.

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