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Immunohistochemical Expression of Survivin in Colorectal Adenomas and Its Correlation With Grade of Dysplasia - a Cross Sectional Study in a Tertiary Care Centre in South Kerala

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Abstract

Background

Colorectal cancer commonly develops through the adenoma–carcinoma sequence. Survivin, a member of the inhibitor of apoptosis protein family, regulates apoptosis and cell proliferation and is minimally expressed in normal adult tissues. Its re-expression in colorectal neoplasia suggests a role in early tumorigenesis and progression.

Objectives

To evaluate the immunohistochemical expression of Survivin in colorectal adenomas and to assess its association with the grade of dysplasia.

Materials and Methods

This cross-sectional study included 40 cases of colorectal adenomas selected by consecutive sampling after ethical clearance. Clinicopathological details were recorded. Histomorphological assessment was performed, followed by immunohistochemical evaluation of Survivin expression. The expression pattern was analysed and correlated with the grade of dysplasia.

Results

Survivin expression was detected in a significant proportion of colorectal adenomas. A statistically significant increase in Survivin expression was observed with increasing grades of dysplasia, with higher expression noted in high-grade dysplasia compared to low-grade dysplasia.

Conclusion

Survivin expression shows a significant association with increasing grades of dysplasia in colorectal adenomas, supporting its role in early colorectal tumorigenesis. Immunohistochemical assessment of Survivin may help identify adenomas with higher malignant potential.

INTRODUCTION

Colorectal cancer is one of the most common malignancies worldwide and commonly arises through the well-established adenoma–carcinoma sequence.[1, 2, 3] The risk of malignant transformation increases with advancing grades of dysplasia in colorectal adenomas, highlighting the importance of identifying biomarkers that reflect early neoplastic progression.[4, 5, 6]

Survivin, the smallest member of the inhibitor of apoptosis protein family, plays a dual role in regulating apoptosis and cell proliferation. While Survivin expression is prominent during embryonic development, it is largely absent in normal adult tissues. Its re-expression has been demonstrated in a variety of human malignancies, including colorectal neoplasia, suggesting a role in tumor initiation and progression.[7, 8, 9]

Several studies have shown increased Survivin expression in colorectal neoplasms, with higher expression reported in lesions showing advanced dysplasia. This supports the hypothesis that Survivin contributes to the adenoma–carcinoma sequence by promoting cell survival and resistance to apoptosis during early tumorigenesis.

The present study aims to evaluate the immunohistochemical expression of Survivin in colorectal adenomas and to assess its association with the grade of dysplasia, thereby exploring its potential role as a marker of neoplastic progression in colorectal adenomas.

MATERIALS AND METHODS

Study Design

This was a cross-sectional observational study conducted in the Department of Pathology, Pushpagiri Institute of Medical Sciences and Research Centre, Tiruvalla, over a period of 18 months following approval from the Institutional Ethics Committee.

Sample Size

Sample size was calculated based on a previous study by Lin et al., which reported Survivin positivity in 31.7% of colorectal adenomas. Using a confidence level of 95% and a power of 90%, the minimum required sample size was calculated to be 39 cases.[1] Accordingly, 39 histopathologically confirmed colorectal adenomas were included in the study.

Study Population

Histopathologically diagnosed cases of colorectal adenomas received in the Department of Pathology during the study period constituted the study population.

Inclusion and Exclusion Criteria

Inclusion criteria

- Histopathologically confirmed cases of colorectal adenoma.

Exclusion criteria

- Patients who had received chemotherapy and/or radiotherapy prior to tissue sampling
- Recurrent colorectal lesions
- Malignant colorectal neoplasms and non-adenomatous lesions

Immunohistochemistry Method

Formalin-fixed, paraffin-embedded tissue blocks of colorectal adenoma cases were retrieved. Sections of 4-µm thickness were cut and stained with hematoxylin and eosin to confirm histopathological diagnosis and grade of dysplasia. Immunohistochemical staining for Survivin was performed using a monoclonal antibody following standard immunohistochemical protocols.

Survivin expression was assessed by evaluating the percentage of positively stained tumour cells in at least five high-power fields (400× magnification). Cases showing < 10% positive tumour cells were considered negative. Cases with 10–29%, 30–59%, and ≥ 60% positive tumour cells were graded as +, ++, and +++, respectively. Scoring was performed in a blinded manner.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using SPSS version 24. Categorical variables were expressed as frequencies and percentages. The association between Survivin expression and grade of dysplasia in colorectal adenomas was analysed using the Chi-square test. A p value < 0.05 was considered statistically significant

RESULTS

The majority of adenoma cases occurred in patients aged >55 years (85%), with a male predominance (60%). Site-wise distribution showed the rectum and transverse colon as the most commonly involved sites (22.5% each), followed by the descending colon (20%) and sigmoid colon (17.5%).(Table 1)

Table 1: Demographic and Clinicopathological Profile of Colorectal Adenomas (n = 40)

Parameter	Category	Number of Cases (%)
Age (years)	≤55	6 (15.0)
	>55	34 (85.0)
Gender	Male	24 (60.0)
	Female	16 (40.0)
Site	Rectum	9 (22.5)
	Transverse colon	9 (22.5)
	Descending colon	8 (20.0)
	Sigmoid colon	7 (17.5)
	Ascending colon	5 (12.5)
	Cecum	2 (5.0)

Based on histological grading, low-grade dysplasia (LGD) was observed in 24 cases (60%), while high-grade dysplasia (HGD) was present in 16 cases (40%). Regarding histological type, tubulovillous adenoma was the most common (50%), followed by tubular adenoma (42.5%) and villous adenoma (7.5%). (Table 2)

Table 2: Distribution of Adenoma Type and Grade of Dysplasia (n = 40)

Adenoma Type	Number of Cases (%)
Tubulovillous	20 (50.0)
Tubular	17 (42.5)
Villous	3 (7.5)

Grade of Dysplasia	Number of Cases (%)
Low-grade dysplasia (LGD)	24 (60.0)
High-grade dysplasia (HGD)	16 (40.0)

Survivin expression was detected in a majority of adenoma cases and showed a significant association with the grade of dysplasia (Fig 1,2,3). In LGD, Survivin expression was predominantly low, with score 1+ in 54.2%, score 2+ in 41.7%, and score 3+ in 4.2% of cases. In contrast, HGD showed higher Survivin expression, with score 2+ in 62.5% and score 3+ in 37.5% of cases, and no cases with score 1+. This association between Survivin expression and grade of dysplasia was highly statistically significant ($\chi^2 = 15.595$, $df = 2$, $p < 0.001$). (Table 3)

Table 3: Survivin Expression in Colorectal Adenomas and Its Association with Dysplasia Grade (n = 40)

Dysplasia Grade	Survivin Score 1+	Survivin Score 2+	Survivin Score 3+	Total
Low-grade (LGD)	13 (54.2%)	10 (41.7%)	1 (4.2%)	24
High-grade (HGD)	0 (0%)	10 (62.5%)	6 (37.5%)	16
Total	13	20	7	40
$\chi^2 = 15.595$, df = 2, $p < 0.001$				

DISCUSSION

Colorectal adenomas represent the key precursor lesions in the adenoma–carcinoma sequence, and identifying molecular markers associated with dysplasia is critical for early detection and risk stratification.[10, 11, 12] In the present study, Survivin expression in adenomas was significantly associated with the grade of dysplasia, with high-grade dysplasia (HGD) cases showing markedly higher Survivin scores compared to low-grade dysplasia (LGD). This suggests that Survivin may contribute to early tumorigenic changes by promoting cell survival and resistance to apoptosis, thereby identifying adenomas with higher malignant potential.

Our findings are consistent with several international studies. Lin et al. (2015) reported Survivin positivity in 30–35% of colorectal adenomas, with higher expression in lesions exhibiting advanced dysplasia, mirroring our observation of increased expression in HGD.(1) Similarly, a study by Hiroshi Kawasaki et al. (2001) demonstrated a stepwise increase in Survivin expression from low- to high-grade adenomas, supporting the role of Survivin as an early biomarker in the adenoma–carcinoma progression.[13] The concordance between our study and these reports underscores the reproducibility of Survivin as a marker of dysplasia across populations.

In contrast, some studies have reported lower overall expression in adenomas or weaker correlation with dysplasia grade. These differences may be attributed to variations in antibody clones, immunohistochemical scoring criteria, sample size, and inclusion of mixed adenoma subtypes. For instance, studies including predominantly tubular adenomas may report lower Survivin positivity compared to studies with a higher proportion of tubulovillous or villous adenomas, which tend to exhibit greater dysplastic changes.[14, 15, 16]

Mechanistically, Survivin's overexpression in HGD adenomas aligns with its dual role in apoptosis inhibition and cell cycle regulation, facilitating clonal expansion of dysplastic epithelial cells.[17, 18, 19] This provides a biological rationale for its utility in risk stratification of adenomas, potentially identifying lesions more likely to progress toward carcinoma.

Overall, the significant association between Survivin expression and dysplasia grade in our study reinforces its potential as a prognostic biomarker in colorectal adenomas, particularly in tertiary care settings in India where early identification of high-risk adenomas can guide surveillance and intervention strategies

CONCLUSION

Survivin expression in colorectal adenomas increases significantly with higher grades of dysplasia, highlighting its potential as a marker for identifying high-risk adenomas.[20,21] This study provides region-specific data from South India, reinforcing the role of Survivin in early malignant transformation and supporting its use in risk stratification and targeted surveillance of adenomatous lesions.

Declarations

Take-home message

Survivin immunoexpression can help identify adenomas with higher malignant potential, guiding early intervention and follow-up strategies

SOURCE OF SUPPORT

Nil

CONFLICT OF INTEREST

None declared.

AUTHORS' CONTRIBUTIONS

- **Concept and design:** Shemeera Saidalavi Vellolipadikkal
- **Data collection and analysis:** Shemeera Saidalavi Vellolipadikkal
- **Histopathological evaluation:** All authors
- **Manuscript drafting:** Shemeera Saidalavi Vellolipadikkal
- **Critical revision:** All authors

All authors read and approved the final manuscript.

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DECLARATIONS

Ethics approval and consent to participate

The study was conducted after obtaining approval from the Institutional Ethics Committee of Pushpagiri Institute of Medical Sciences and Research Centre, Tiruvalla (IEC Reg No. with DHR : EC/NEW/Inst/2020/1188). The study was performed in accordance with the ethical standards of the institutional research committee and the principles of the Declaration of Helsinki. As the study was based on archived histopathological specimens, patient confidentiality and anonymity were strictly maintained.

Consent for publication

Not applicable. The study does not contain any identifiable personal data or patient images requiring consent for publication.

Availability of data and materials

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Shemeera Saidalavi Vellolipadikkal conceived and designed the study. Data collection, histopathological evaluation, and analysis were performed by the authors. Shemeera Saidalavi Vellolipadikkal drafted the manuscript. All authors critically revised the manuscript and approved the final version.

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Figures

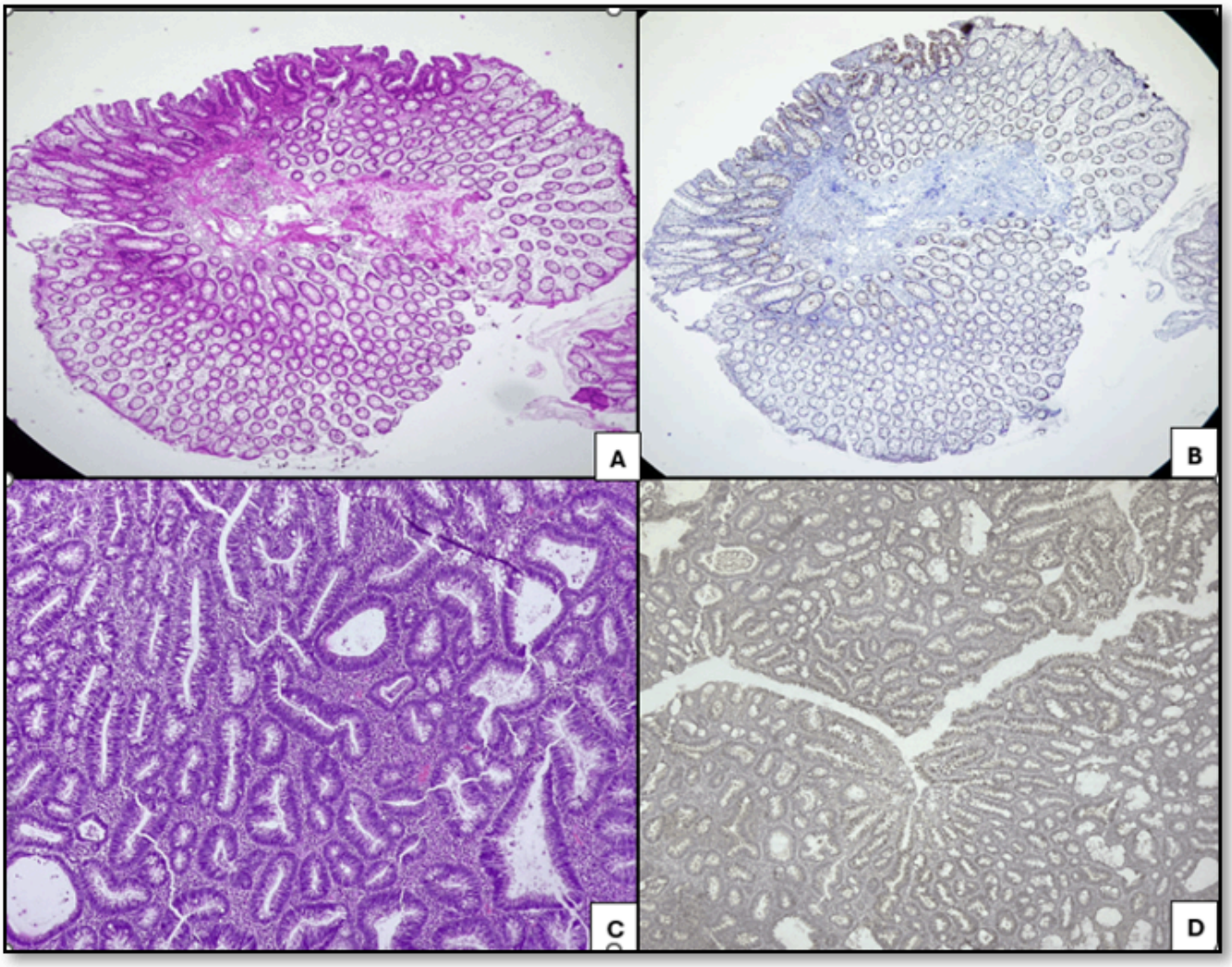


Figure 1

A:Tubular adenoma with focal LGD (H&E,4x), B: Survivin score 2+ in tubular adenoma with LGD (4x), C: Tubular adenoma with HGD(H&E,10x), D: Survivin score 3+ in tubular adenoma with HGD(10x)

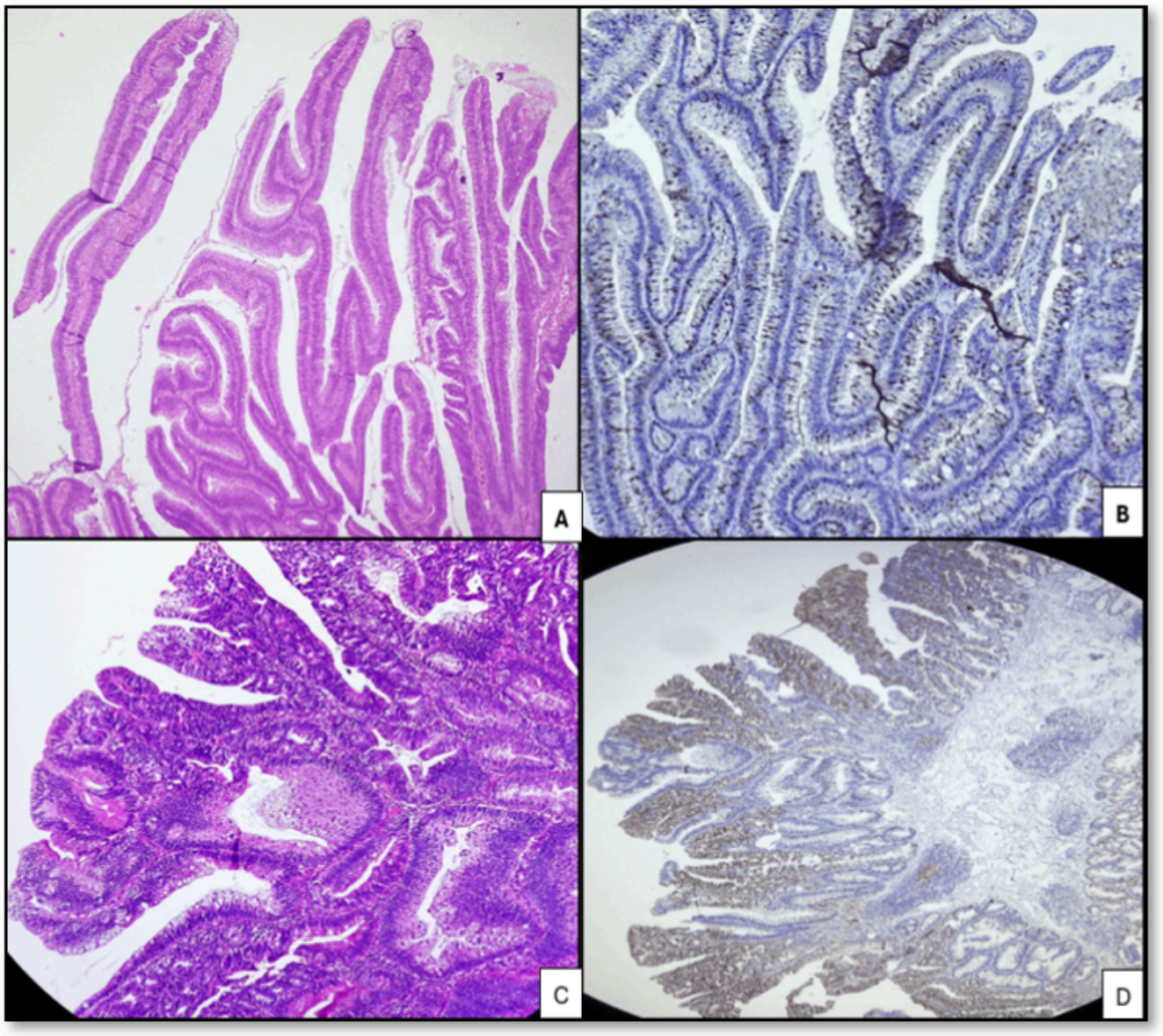


Figure 2

A: Villous adenoma with LGD (H&E,10x), B: Survivin score 2+ in Villous adenoma with LGD (10x), C: Villous adenoma with LGD (H&E,10x), D: Survivin score 2+ in Villous adenoma with LGD (10x)

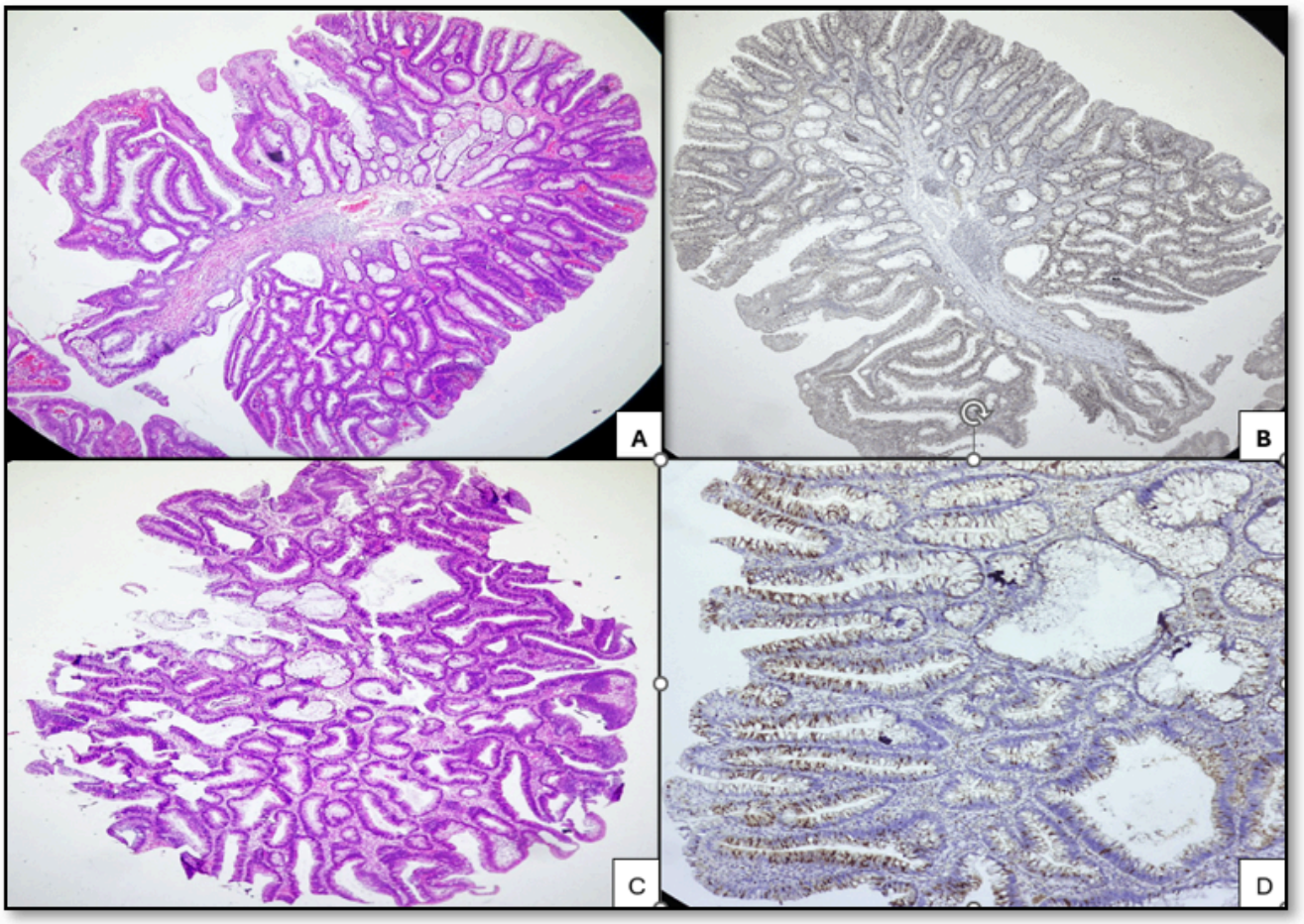


Figure 3

A: Tubulovillous adenoma with LGD (H&E,4x), B: Survivin score 2+ in Tubulovillous adenoma with LGD (4x), C: Tubulovillous adenoma with HGD (H&E,10x), B: Survivin score 3+ in Tubulovillous adenoma with HGD (10x)