e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com doi: 10.25258/ijpqa.16.12.85

International Journal of Pharmaceutical Quality Assurance 2025; 16(12); 512-518

Original Research Article

Expression of Beta-Catenin in Colorectal Carcinoma: An Institutional Study

Jasnita Bhoi[1], Gitimadhuri Dutta[2], Saktidhar Parida[3], Sudarshan Sethy[4]

[1]Senior Resident, Department of Pathology, PRM Medical College, Baripada, Odisha, India
[2]Professor, Department of Pathology, VIMSAR, Burla, Odisha, India
[3]EX Additional Director II, Department of Health & Family Welfare, Government of Odisha, India
[4]Associate Professor, Department of General Surgery, VIMSAR, Burla, Odisha, India

Received: 19-10-2025 / Revised: 18-11-2025 / Accepted: 19-12-2025
Corresponding Author: Dr. Gitimadhuri Dutta
Conflict of interest: Nil

Abstract:

Background: Colorectal carcinoma is one of the most important public health problems causing significant morbidity and mortality globally and here the main cause of mortality is tumor invasion and metastasis. Pathogenesis of colorectal is a multistep process during which different molecular pathways come into play. Beta-catenin, a central molecule of Wnt signaling system, expresses in epithelial cells as two main forms; membrane localization and nuclear accumulation. This beta catenin is responsible for cell proliferation, differentiation and enhanced survival of colorectal epithelial cells. Membrane localization can be detected in normal cells and tumor lineage whereas nuclear accumulation is exclusively detected in immature and tumor cells

Methods: All radical excised specimens and colonoscopy biopsies were collected from histopathology section and immunohistochemistry was done in the Department of Pathology, VIMSAR, Burla from August 2022 to July 2024.

Results: 60 cases of colonic carcinoma were received from Department of General Surgery of which 29 were colectomy and 31 were endoscopic biopsy specimens. All were of adenocarcinoma with M:F ratio 1.26:1 and most common site being rectum. High membranous expression was seen in 67% cases whereas 60% cases showed nuclear positivity.

Conclusion: Expression of beta catenin shows gradual transition from predominant membranous expression to subsequent positivity in cytoplasmic and nuclear location as we progress from low histological grade to high grade of colorectal carcinoma. This property of beta catenin helps to detect the cases earlier and initiate early treatment.

Keywords: colorectal carcinoma, beta catenin expression.

Introduction

Colorectal carcinoma is the fourth most common cause of cancer in males and third most common cause in females.[1] It is one of the three most frequently encountered malignancy and second leading cause of cancer-related death in the world.[2] As per World Health Organization GLOBOCAN database, there were 1.9 million estimated new colorectal carcinoma cases and 904000 deaths due to it in 2022.[3] Annual incidence rate for colorectal carcinoma in male is 5.36 per 100,000 population and 4.3 per 100,000 population in females in India.[4] Prognosis of colorectal carcinoma patients depends on tumor size, histologic type, tumor grade, lympho-vascular invasion, lymph node involvement and metastatic level.[5] WNT/β-Catenin signaling pathway is a conserved pathway mediating tumorigenesis. The earliest genetic event in colorectal tumorigenesis is mutation of adenomatous polyposis coli (APC) gene; which leads to pathologically increased cytoplasmic beta-catenin. This can be translocated to the nucleus where it functions as a transcription factor and promotes cellular proliferation, differentiation and enhanced survival of colorectal epithelial cells. [6,7] There are two broad categories of colorectal cancer risk factors, non-modifiable and modifiable risk factors. Non-modifiable risk factors are ethnicity, sex, age, hereditary mutations and inflammatory bowel disease, among modifiable risk factors are sedentary lifestyle, obesity, diet, smoking and alcohol consumption. [8,9] Beta-catenin is an important component of the WNT/β-catenin pathway. It is a multifunctional protein which is encoded by the CTNNB1 gene. Increased nuclear β-catenin expression is a sign of aberrant beta-catenin signaling pathway activation which promotes tumor progression [10]

Materials and Methods

The present study was conducted in the Department of Pathology VIMSAR Burla, Odisha from August

2022 to July 2024. It was approved by institutional Ethics Committee. This study included 60 cases of colorectal carcinoma. Inclusion criteria were all radical excision specimens of histologically confirmed cases of colorectal carcinoma and colonoscopy biopsy specimen of colorectal carcinoma. Exclusion criteria were all non- neoplastic lesions. The parameters included in our study were age, sex, location of tumor, histologic type, histological grade, TNM stage, CEA level, lymph node metastasis, lymphovascular invasion and perineural invasion. Immunohistochemistry evaluation of β-catenin was done on formalin fixed paraffin embedded tissue sections on poly L-lysine coated slides by using polymers in two steps. Antigen retrieval from tissue sections is done by adding the proteolytic enzyme followed by application of wet heat in a microwave oven. An unconjugated primary antibody is added to the retrieved antigen followed by secondary antibody which is conjugated with Horse Radish Peroxidase enzyme labelled to a polymer. The chromogen 3,3 diaminobenzidine is oxidized in presence of hydrogen peroxidase releasing nascent oxygen which impart brown colour to the tissue. Normal colorectal tissue was taken as internal positive control from the same block under study. Histologically diagnosed section from fibromatosis block was taken as external positive control. Negative control for beta catenin was achieved by omitting primary antibody on the same block. The beta catenin staining was evaluated using regular light microscope by a pathologist who was blind to the clinical and pathological data. All membranous, cytoplasmic and nuclear staining were evaluated separately.

Statistical Analysis: The data entry was done using Microsoft Excel spread sheet 2010 and statistically analyzed using SPSS version 22. The groups were tested for statistical association using chi-square test and Fisher's exact test. A p-value of less than 0.05 was considered statistically significant.

Results

A total number of 60 cases with colorectal carcinoma were evaluated. The age group of patients ranged from age 20 years to 88 years with a mean age of 54.28 years. Maximum numbers of patients 30% cases were in the age group of seventh decade, followed by 21.66% in the 6th decade age group. Lowest number of cases 1.66% were present in two age group second decade and ninth decade. (Table - 1) Out of 60 cases 24 cases (43%) cases were female; whereas 33(57%) cases were male. Most common lesions were seen in colon 53.33% cases, followed by ascending colon (15%), 10% lesions were located in rectosigmoid junction, 8.33% lesions were seen in sigmoid colon and 6.66% lesions were seen both transverse and descending colon. In our study we found 50% cases belonged to grade 1, 43.33% cases were grade 2 and 6.66% cases were grade 3. Maximum number of cases (70%) belonged to stage II followed by 16.66% cases were stage III and 13.33% cases were stage I. In our study we found 66.66% cases were showing lympho-vascular invasion and 30% cases showed perineural invasion. Only 16.66% cases showed lymph node metastasis and remaining 83.33% cases showed no nodal metastasis. 70% cases had CEA level <5 ng/ml and 30% cases had CEA level >5 ng/ml. 66.66% cases showed membranous beta catenin expression and 33.33% cases showed negative expression. In case of cytoplasmic expression of beta-catenin, we found 50% cases showed cytoplasmic positivity. 25% cases showed nuclear positivity of beta catenin expression and 75% cases showed negative expression. Membranous expression levels of beta catenin were preserved in 83.33% cases of those patients who are less than 50 yrs old, where as those who are more than 50 yrs old 50% cases had preserved membranous expression. Increased cytoplasmic expression of beta catenin were seen in 58.33% cases those who were less than 50 years, while those who were above 50 years 75% cases showed cytoplasmic expression. Increased nuclear expression were seen in 58.33% cases of those who were less than 50 years, while those who are above 50 years 75% cases showed high nuclear expression. These results were not found to be statistically significant. In our study out of total 34 male patients, 47.05% cases showed preserved membranous expression of beta-catenin, but in case of female it was seen in 73.04% 0f cases. 22 out of 34 male patients (64.74%) male patients had high cytoplasmic expression of beta catenin, whereas it was seen in 10 out 26 (38.46%) of female patients. Higher nuclear expression of beta-catenin was seen in 32.35% male patients and in 62.23% of female patients. But these results were not found to be statistically significant. Preserved membranous expression of carcinoma in ascending colon was seen in 45% cases, in both transverse and descending colon it was seen in 50% cases in both, in sigmoid colon it was seen in 36% cases and in rectum it was seen in 31% cases. The result was statistically not significant. Increased cytoplasmic expression observed in ascending colon was 33%, in both transverse and descending colon it was 25% in each case. In sigmoid colon cytoplasmic expression was 73% and in rectum it was 63%. The result was statistically significant with p value 0.05. Increased nuclear expression observed in ascending colon was 33% of cases, in both transverse and descending colon it was expressed in 25% cases in each. In sigmoid colon it was expressed in 73% cases and in rectum it was expressed in 63% cases. The result was statistically significant with p value 0.05. Increased nuclear expression observed in ascending colon in 33% cases, in sigmoid colon it was expressed in 64% cases and in rectum it was expressed in 56% cases. This result was statistically significant with p value 0.01. Preserved membranous expression of beta catenin in grade-1 carcinoma was 83%, in grade -2 it was 62%,

while no cases with grade 3 carcinoma had membranous expression. This result was statistically significant with p value 0.04. (TABLE-2) High cytoplasmic expression of beta catenin in grade 1 was 67%, in grade -2 it was 77%, in grade -3 it was 50%. This result was statistically significant with p value of 0.02. Increased nuclear expression of beta-catenin in grade -1 was 33, in grade -2 it was 19%, and in grade 3 it was 75%. This result was statistically significant with p value of 0.03. Preserved membranous expression of beta catenin in stage I was 88%, in stage II it was 64%, in stage III, it was 10%. This result was statistically significant with a p value of 0.001. (Table-3). Increased cytoplasmic expression in stage I was 25%, in stage II it was 60%, and in stage III it was 70%. This result was statistically significant with p value of 0.008. Increased nuclear expression in stage I was 13%, in stage II it was 24% and in all stage III cases (100%) had increased nuclear expression of beta catenin. This result was statistically significant with p value of 0.008. 22 out of 40 cases (55%) having lympho-vascular invasion had preserved membranous expression. 17 out of 40 cases (42%) having lympho-vascular invasion showed increased cytoplasmic expression of beta catenin. 12 out of 40 cases (30%) having lympho-vascular invasion showed nuclear beta catenin expression. There was no statistical correlation between lympho-vascular invasion and beta-catenin expression. 8 out of 10 (80%) cases with nodal metastasis showed preserved membranous expression and cases without metastasis (20%) had preserved membranous expression. 4 out of 10 (40%) cases with nodal metastasis showed increased cytoplasmic expression and cases without metastasis (24%) had increased cytoplasmic expression. 3 out of 10 cases (30%) cases with nodal metastasis showed high nuclear expression and cases without metastasis (10%) had high nuclear expression. There was no statistically significant association between lymph node metastasis and beta catenin expression.

Table 1: Age distribution of all cases of colonic carcinoma(n=60)

Age group in years	Numbers	Percentage (%)
11-20	1	1.66
21-30	3	5.00
31-40	10	16.66
41-50	10	16.66
51-60	13	21.66
61-70	18	30.00
71-80	4	6.66
81-90	1	1.66
Total	60	100

Table 2: Correlation of β-catenin expression in colonic carcinoma with histological grades

Histological Grades	Total	Membranous expression			Cytoplasmic expression			Nuclear expression		
		Preserved	Reduced	p-value	Low	High	p-value	Low	High	p-value
Grade-1	30	25 (83%)	5 (17%)	0.04	10 (33%)	20 (67%)	0.02	20 (67%)	10 (33%)	0.03
Grade-2	26	16 (62%)	10 (38%)		6 (23%)	20 (77%)		21 (81%)	5 (19%)	
Grade-3	4	0 (0%)	4 (100%)		2 (50 %)	2 (50%)		1 (25%)	3 (75%)	

Table 3: Correlation of β-catenin expression in colonic carcinoma with pathological stages

Patho-Logical Stages	Total	Membranous expression			Cytoplasmic expression			Nuclear expression		
		Preserved	Reduced	p-value	Low	High	p-value	Low	High	p-value
Stage-I	8	7 (88%)	1 (12%)	0.001	6 (75%)	2(25%)	0.008	7(87%)	1(13%)	0.008
Stage-II	42	27 (64%)	15 (36%)		17(40%)	25(60%)		32(76%)	10(24%)	
Stage-III	10	1 (10%)	9 (90%)		3(30%)	7(70%)		0(0%)	10(100%)	

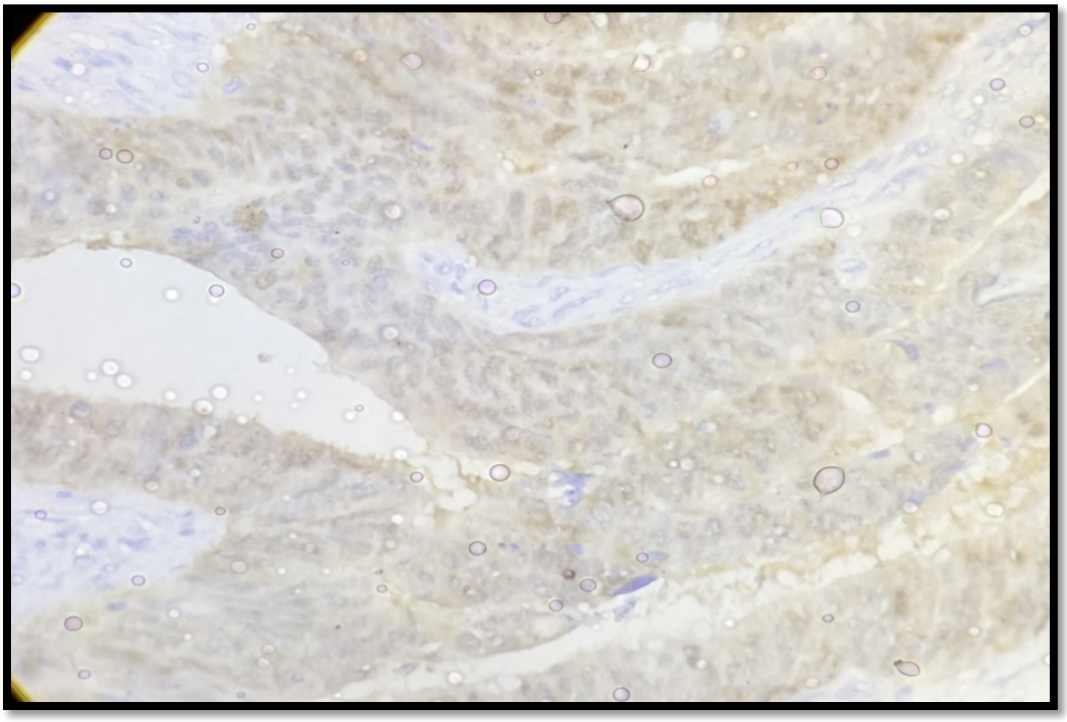

Figure 1: Adenocarcinoma of Colon, membranous and cytoplasmic expression of β-catenin, Score 2+, IHC- 400X

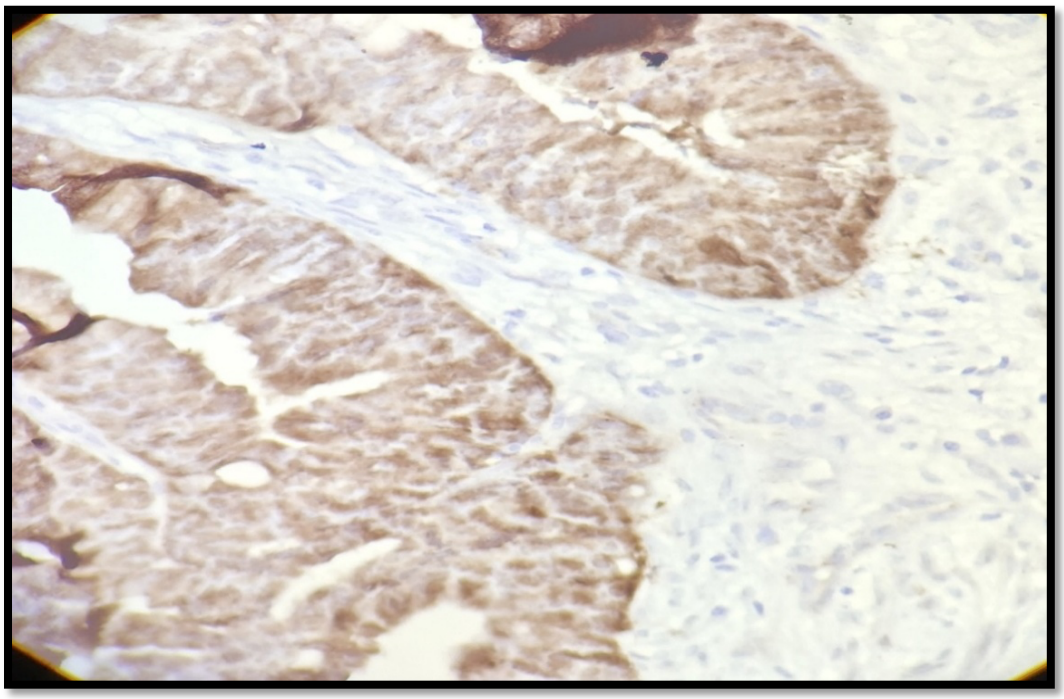

Figure 2: Adenocarcinoma of Rectum, cytoplasmic and nuclear expression of β-catenin, Score 3+, IHC-400X

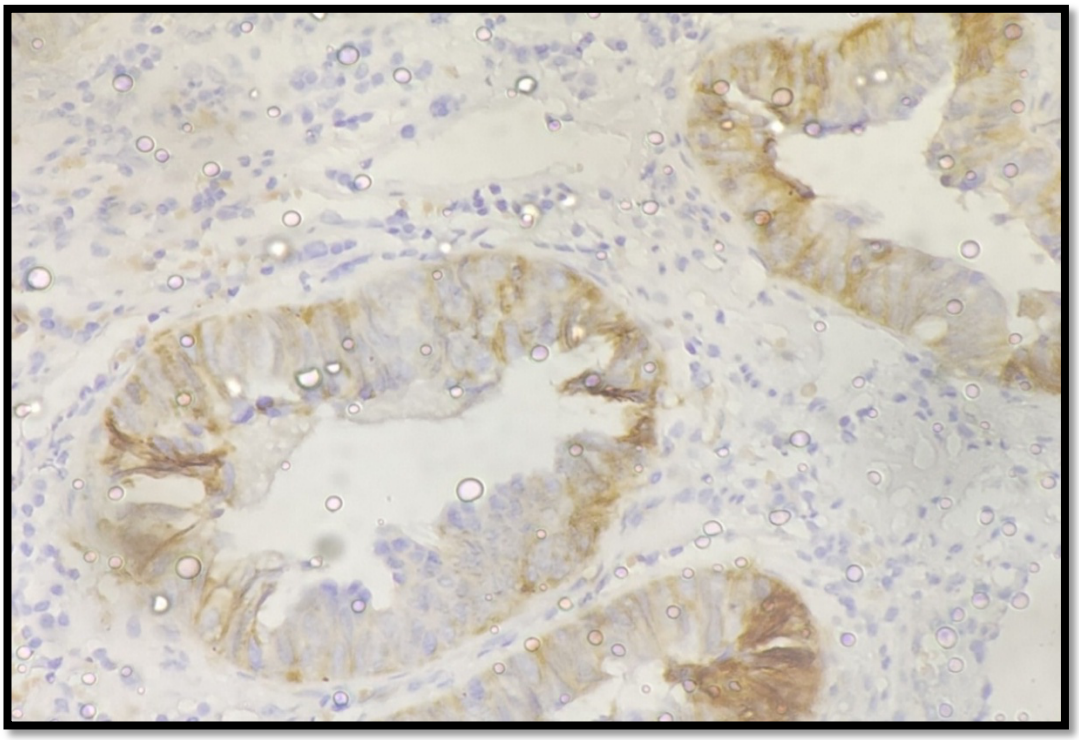

Figure 3: Adenocarcinoma of Ascending Colon, membranous and cytoplasmic expression of β-catenin, Score 2+, IHC-400X

Discussion

One of the main causes of death due to carcinoma is colorectal cancer and beta-catenin plays a significant part in disease development. Beta-catenin has been identified as an integral membrane protein which in association with E-cadherin facilitates cell to cell interactions. The WNT signaling pathway regulates beta-catenin's function. APC and beta-catenin gene mutations result in an excess of intracellular beta-catenin accumulation, which translocate to the nucleus and activates a transcription factor, leading to unchecked growth and carcinogenesis. There is typically no intracellular buildup of beta-catenin since it was broken down by APC-β-catenin complex.[11] In this present study various patterns of IHC expression of beta-catenin in association with age, sex, site, histological grade, pathological stage, LVI, PNI, lymph-node metastasis was studied.

For beta-catenin correlation and statistical analysis the patients were divided into two groups: a-< 50years and b-> 50 years. In our study we found that patients with >50 years of age showed high cytoplasmic and nuclear expression of beta-catenin than the patients with <50 years of age. Gao et al studied beta catenin expression in relation to age. They divided their cases into two age groups of <60 years and >60 years. They found that >60 years of patients had more cytoplasmic and nuclear beta catenin expression.[12] Shue Li et al also divided 160 cases into two age groups one <60 years and others >60 years. They also found >60 years of patients had more cytoplasmic and nuclear beta-catenin expression.[6] Out of 60 cases, there were 34 male patients 26 female patients in our study. The male to female ratio in our study was 1.26:1 with overall male predominance was seen. Increased cytoplasmic expression of beta-catenin was noted in males as compared to females, whereas higher nuclear beta-catenin expression was seen in female patients. The membranous beta-catenin level was preserved more in females in our study. There was no correlation found between beta-catenin expression and sex. Similar to our study, Gao et al.'s analysis of 181 cases of colorectal cancer included 105 male and 76 female patients with a M:F ratio of 1.3:1. In their cases, female patients had greater nuclear beta-catenin expression and male patients had more membranous and cytoplasmic expression.[12] Yoshida et al.[13] studied 201 cases of colorectal carcinoma, of which 120 cases were male and 81 cases were female with M:F ratio of1.4:1.This study was not consistent with our study, and it revealed higher levels of beta-catenin expression in females.

Out of 60 cases of adenocarcinoma of colon maximum number of cases were located in rectum (53.33%), followed by sigmoid colon 18.33% and ascending colon 15% in our study. Higher cytoplasmic and nuclear expression was observed in rectum followed by sigmoid colon. This result was statistically significant with p value 0.001. Gao et al [12] in their study they found rectal carcinoma had higher level of nuclear and cytoplasmic expression of beta-catenin. This study was similar to our study.

Wanitsuwan W et al. [7] in their study they found colonic mases showed higher nuclear expression of beta-catenin. This was not concordant with our study.

In this present study out of 60 cases of adenocarcinoma maximum number of cases (30) 50% were grade-1, followed by grade-2. Patients with grade-1 and grade-2 carcinoma had high membranous and cytoplasmic of beta-catenin than grade-3 tumors. Where as in grade-3 cases we got high nuclear expression of beta-catenin, which was statistically significant with p value 0.03. Gao et al. had divided the tumor grades into two groups. So out of 181 cases of colorectal carcinoma group 1 had 132 cases and group 2 had 49 cases. They found increased cytoplasmic expression in grade 1 and grade 2, whereas high nuclear expression was found in grade-3 tumor. Out of 60 cases of adenocarcinoma in our study 42 cases (70%) belonged to stage II, followed by 10 cases (16.66%) stage III and 8 cases (13.33%) were stage I. The cases with stage I and stage II showed increased membranous and cytoplasmic expression than stage III. The stage III cases showed increased nuclear expression, which was statistically significant with p value 0.001. In the study of Gao et al. the carcinoma cases with stage I and stage II had more preserved membranous expression and high cytoplasmic positivity. Whereas in case of stage III and stage IV tumors there is a greater number of nuclear expression than cytoplasmic expression. So the study of Gao et al. was in concordant with our study. In our study out of 60 cases 40 cases (66%) show lympho-vascular invasion. In our study out of 60 cases 18 cases showed perineural invasion. Most of the patients having lympho-vascular invasion showed preserved membranous expression than cases without lympho-vascular invasion. These cases showed high cytoplasmic expression. But few cases with lympho-vascular invasion showed nuclear positivity. Similarly, the cases with perineural invasion showed preserved membranous as well as high cytoplasmic expression than that without perineural invasion. But nuclear expression was high in the carcinoma cases which were without perineural invasion. In Gao et al. [12] study out 181 cases only 3 cases showed lympho-vascular invasion. Out of 3 cases only one case showed preserved membranous expression. But no cases showed either cytoplasmic or nuclear expression. This study was not concordant with our study. In our present study out of 60 cases, only 10 cases presented with lymph node metastasis and 50 cases were without lymph node metastasis because maximum cases in our study were colonoscopic biopsy specimen. The cases with lymph node metastasis showed preserved membranous and high cytoplasmic expression of beta-catenin as compared to cases without lymph node metastasis. In the study of Wanitsuwan et al. [7] he found that cases with lymph node metastasis had higher cytoplasmic and nuclear expression as compared to that of without lymph node metastasis.

Conclusion

The present study demonstrates the changes in the expression of beta-catenin which shows a gradual transition from a predominant membranous expression to subsequent positivity in cytoplasmic or nuclear location as we progress from low histological grade to high grade of colorectal carcinoma. This property of beta-catenin helps to diagnose the cases earlier, which in turn can help to initiate early treatment.

References

1. The History of cancer, American Cancer society, Cancer.org/1.800.227.2345
2. Bhattacharya I, Barman N, Maiti M, Sarkar R. Assessment of beta-catenin expression by immunohistochemistry in colorectal neoplasms and its role as an additional prognostic marker in colorectal adenocarcinoma. Med Pharm Rep.2019 Jul;92(3):246-252
3. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024 May-Jun;74(3):229-263. doi: 10.3322/caac.21834. Epub 2024 Apr 4. PMID: 38572751.
4. Asthana, Smita; Khenchi, Rubal; Labani, Satyanarayana,*. Incidence of colorectal cancers in India: A review from population-based cancer registries. Current Medicine Research and Practice 11(2):p 91-96, Mar–Apr 2021. | DOI: 10.4103/cmrp.cmrp_65_20
5. Compton CC. Colorectal carcinoma: diagnostic, prognostic, and molecular features. Mod Pathol. 2003 Apr;16(4):376-88. doi: 10.1097/01.MP.0000062859.46942.93. PMID: 12692203.
6. Li S, Huang M, Liu Q, Wang D, Wu R, Zhang X, Chen W, Duan L. Serum Expression of β-Catenin Is a Potential Detection Marker in Patients with Colorectal Cancer. Dis Markers. 2019 Oct 24;2019:5070524. doi: 10.1155/2019/5070524. PMID: 31781302; PMCID: PMC6855041.
7. Wanitsuwan W, Kanngurn S, Boonpipattanapong T, Sangthong R, Sangkhathat S. Overall expression of beta-catenin outperforms its nuclear accumulation in predicting outcomes of colorectal cancers. World J Gastroenterol. 2008 Oct 21;14(39):6052-9. doi: 10.3748/wjg.14.6052. PMID: 18932285; PMCID: PMC2760180.
8. Sawicki T, Ruszkowska M, Danielewicz A, Niedźwiedzka E, Arłukowicz T, Przybyłowicz KE. A Review of Colorectal Cancer in Terms of Epidemiology, Risk Factors, Development, Symptoms and Diagnosis. Cancers (Basel).

2021 Apr 22;13(9):2025. doi: 10.3390/cancers13092025. PMID: 33922197; PMCID: PMC8122718.
9. Ionescu VA, Gheorghe G, Bacalbasa N, Chiotoroiu AL, Diaconu C. Colorectal Cancer: From Risk Factors to Oncogenesis. Medicina (Kaunas). 2023 Sep 12;59(9):1646. doi: 10.3390/medicina59091646. PMID: 37763765; PMCID: PMC10537191.
10. Yoshida N, Kinugasa T, Ohshima K, Yuge K, Ohchi T, Fujino S, Shiraiwa S, Katagiri M, Akagi Y. Analysis of Wnt and β-catenin Expression in Advanced Colorectal Cancer. Anticancer Res. 2015 Aug;35(8):4403-10. PMID: 26168479.
11. Zhan T, Rindtorff N, Boutros M. Wnt signaling in cancer. Oncogene. 2017 Mar;36(11):1461-1473. doi: 10.1038/onc.2016.304. Epub 2016 Sep 12. PMID: 27617575; PMCID: PMC5357762.
12. Gao ZH, Lu C, Wang MX, Han Y, Guo LJ. Differential β-catenin expression levels are associated with morphological features and prognosis of colorectal cancer. Oncol Lett. 2014 Nov;8(5):2069-2076. doi: 10.3892/ol.2014.2433. Epub 2014 Aug 11. PMID: 25295092; PMCID: PMC4186582.
13. Yoshida N, Kinugasa T, Ohshima K, Yuge K, Ohchi T, Fujino S, Shiraiwa S, Katagiri M, Akagi Y. Analysis of Wnt and β-catenin Expression in Advanced Colorectal Cancer. Anticancer Res. 2015 Aug;35(8):4403-10. PMID: 26168479.