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Original Article

Pathology Section

Analysing Immunohistochemical Co-expression of CDH17, CK7 and CK20 in Lower Gastrointestinal Tumours: A Cross-sectional Study

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ABSTRACT

Introduction: Lower gastrointestinal tract malignancies, especially colorectal malignancy constitute one of the most common malignancies worldwide and most common cause of cancer-related deaths in developed countries. It accounts for third most common malignancy in men and the second most common in women worldwide. In this context, CDH17 and CK20 are emerging markers for diagnosis, prognosis, and for targeted therapy in the future.

Aim: To assess the expression of immunohistochemical markers like CDH17, CK7 and CK20 in lower gastrointestinal tumours.

Materials and Methods: This cross-sectional study was conducted in the Department of Pathology, Chengalpattu Medical College, Chengalpattu, Tamil Nadu, India, for the duration one year six months, April 2020-October 2021. All cases of lower gastrointestinal tract malignancies obtained as small biopsies or resected specimens of about 40 cases were included in this study. For all cases, four sections were taken: one for Haematoxylin and Eosin (H&E) stain and the other three for immunohistochemical stains for CDH17, CK7, and CK20, respectively. The sections were stained using a standard protocol. Histopathological categorisation, pathological staging, and grading of lower gastrointestinal carcinomas were conducted in conjunction with the immunohistochemical markers CDH17, CK7, and CK20. Descriptive statistics, including frequency and percentages, were calculated. The association between categorical variables was analysed by Kruskal-Wallis test.

Results: Among the 40 cases, the expression of the CDH17, CK20, and CK7 markers showed 95.00% positivity (38 cases) for CDH17 and 92.50% positivity (37 cases) for CK20, whereas CK7 was found to be negative in 95.00% (38 cases) of the cases.

Conclusion: The expression of CDH17 and CK20 in lower gastrointestinal malignancies, especially in the colorectum, was strong and diffuse. In contrast, the CK7 marker was not expressed in lower gastrointestinal malignancies. Thus, the IHC markers CDH17 and CK20 can be routinely employed as cocktail markers in lower gastrointestinal malignancies, especially in colorectal carcinoma of unknown primary origin.

Keywords: Immunostaining, Pathological classification, Prognostic factors

INTRODUCTION

Lower gastrointestinal tract malignancies, especially colorectal malignancy account for the third most common malignancy in men and the second most common in women worldwide [1]. The annual incidence rates for rectal cancer and colon cancer in men are 4.1 and 4.4 per 10,000, respectively, whereas for colon cancer in women is 3.9 per 100,000 [2]. Liver-intestine Cadherin 17 (CDH17) is a cell-cell adhesion mediator in the intestinal epithelium and is a calcium-dependent transmembrane glycoprotein. CDH17 expression has been reported in colorectal, gastric, and pancreatic malignancies, with very less expression in other tumours. About 96% of colorectal adenocarcinomas stain strongly and diffusely for CDH17. Assessing CDH17 is helpful in detecting prognosis.

Cytokeratin 7 (CK 7) and Cytokeratin 20 (CK 20) are low molecular weight cytokeratins found in the gastrointestinal epithelium and in their neoplasms [3]. The CK 7/CK 20 panel is useful for identifying the site of origin; CK 20 stains positive in lower gastrointestinal malignancies, whereas CK 7 stains negative [4]. Cadherins are cell-cell adhesion molecules characterised by several calcium-binding motifs in the extracellular domain, a single transmembrane region, and a carboxyl intracellular domain [5]. This family of proteins plays an important role in maintaining tissue structure and morphology in a normal state, whereas the loss of cadherin expression correlates with more aggressive behaviour in some carcinomas [6,7]. CDH17 is a member of the cadherin superfamily that shows unique structural features. It has seven 7 extracellular cadherin repeats, compared to five in classic cadherins [8]. CDH17 is a novel diagnostic marker for gastrointestinal tract carcinoma, demonstrating greater sensitivity than CDX2 in colon cancers [9].

In the intestinal epithelial cells, E-cadherin, one of the classic cadherins, whereas cadherin 17 is evenly distributed along the lateral contact areas [10]. Cadherin 17 expression is thought to be regulated by CDX2, an intestine-specific caudal-related homeobox transcription factor that plays an important role in the regulation of the development and homeostasis of intestinal epithelial cells, and in the maintenance of the intestinal phenotype [11]. The tissue distribution of cadherin 17 differs by species; it is expressed in the liver and intestinal epithelial cells of rats, but in mice and humans, its expression is almost exclusively limited to the epithelial cells of both embryonic and adult small intestine and colon, with no detectable expression in the liver and stomach [12]. Current information indicates that, similar to CDX2, cadherin 17 can be used as an immunohistochemical marker for tumours arising in the gastrointestinal tract. With the exception of adenocarcinomas of the stomach, the sensitivity of cadherin 17 for these tumours is higher than that of CDX2.

Cytokeratins (CKs), members of the intermediate filament family alongside vimentin, desmin, neurofilament, and glial filament, are proteins expressed by epithelial cells. The combined expression patterns of CK7 and CK20 have been extensively studied in various primary and metastatic carcinomas. A high proportion of colorectal

cancer cases exhibit CK7+ (around 17%) and CK20- (up to 19%), as noted in some studies. This indicates that the absence of the "typical" expression profile for this location, i.e., CK20+/CK7-, in metastases does not preclude the origin of the primary tumour in the colon [13]. CK20 is considered as one of the markers of colonocyte differentiation; one reason for its reduced expression may be tissue dedifferentiation during the process of carcinogenesis. Although rare, primary adenocarcinomas arising in Anal Gland Carcinoma (AGC) may occasionally enter the differential diagnosis of colorectal cancer. AGC typically presents as infiltrating, haphazard glandular structures within the wall of the anus, devoid of an identifiable luminal precursor lesion. They characteristically show diffuse expression of CK7 but are negative for CDX2 and, with rare exceptions, CK20 [14].

Aim of the present was to study the histopathological features of lower gastrointestinal tract malignancies and also to study the expression of IHC markers CDH17, CK7, and CK20 in lower gastrointestinal tract malignancies.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Pathology, Chengalpattu Medical College, Chengalpattu, Tamil Nadu, India. It was done for one year six months, April 2020-October 2021. The Institutional Ethical Committee granted permission for the study (Ethical committee number-5945/2020). Cases positive for lower gastrointestinal malignancies were selected from the tumour register for this study. All cases of lower gastrointestinal tract malignancies obtained from small biopsies or resected specimens, totaling around 40 cases, were included in the study group. The most representative paraffin-embedded tissue blocks were chosen. Four sections were taken: one for H&E staining and the other three for IHC stains CDH17, CK7, and CK20 using a standard protocol.

Inclusion criteria: Small biopsies and resected specimens from the lower gastrointestinal tract (from the caecum to the anal canal) diagnosed as carcinoma were included in the study.

Exclusion criteria: Biopsies from known patients with gastrointestinal malignancies who underwent preoperative therapeutic chemotherapy or radiotherapy, biopsies diagnosed as lymphomas in the lower gastrointestinal tract, and non neoplastic lesions of the lower gastrointestinal tract were excluded from the study.

Study Procedure

Staging of the tumour was not included, since lymph nodes were not studied. Histopathological categorisation, pathological staging, and grading of lower gastrointestinal carcinomas were assessed based American Joint Committee on Cancer (AJCC) 8th edition [15] and the World Health Organisation (WHO) classification [16]. The clinical parameters studied included age, gender, and site.

Immunohistochemical staining of CDH17, CK7, and CK20 was assessed based on a scoring system accessed by staining intensity and the percentage of cells taking up the stain. Cells were considered positive for CK20 and CK7 when distinct yellow to brown staining was identified in the cytoplasm and/or cell membrane. The percentage of positive cells was recorded using a semiquantitative method according to a scale from 1 to 4:

- Score 4 (staining in >50% of tumour cells),
- Score 3 (staining in 20-50% of cells),
- Score 2 (staining in 5-20% of cells),
- Score 1 (staining in ≤5% of cells) [17].

Scoring for CDH17 was as follows:

- 0 (no detectable staining);
- 1+ (25% positive cells);
- 2+ (25-49% positive cells);
- 3+ (50-74% positive cells);
- 4+ (75% or more positive cells).

In cells with positive staining, the staining was intense and uniform, so intensity was not factored into the scoring [18].

STATISTICAL ANALYSIS

The statistical analysis was done by using Statistical Package for the Social Sciences (SPSS) version 20.0. Descriptive statistics, including frequency and percentages, were calculated. The association between the categorical variables was analysed using the Kruskal-Wallis test.

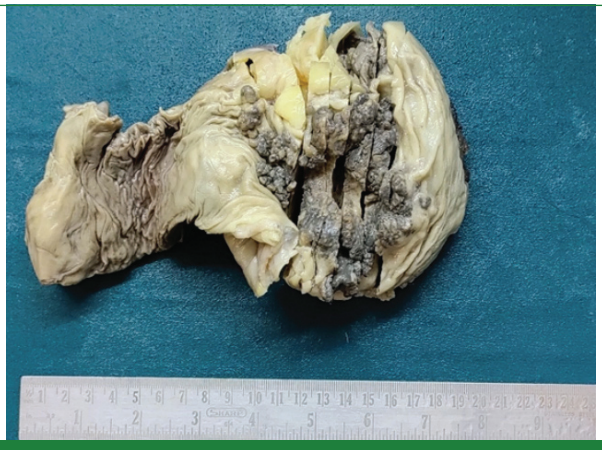
RESULTS

An analysis of 40 cases of colorectal carcinomas was done which included small biopsy specimens, hemicolectomies, and abdominal perineal resections. The patients were divided into five age groups: under 40 years, 41-50 years, 51-60 years, 61-70 years, and over 70 years. The median age group in this study population was 59 years [Table/Fig-1]. In terms of gender distribution, 25 (62.5%) participants were males and 15 (37.5%) were females. This study shows a higher incidence of lower gastrointestinal tumours among males. Lower gastrointestinal tumours were more commonly seen in the rectum 20 cases (50%), followed by the colon 15 cases (37.5%), caecum 3 cases (7.5%) and hepatic flexure 2 cases (5.0%). The study sample included 40 specimens, of which 20 (50.0%) were hemicolectomy specimens, 17 (42.50%) were rectal biopsy specimens, and 3 (7.50%) were Abdominoperineal Resection (APR) specimens [Table/Fig-2-4]. The most common histopathological diagnosis observed in this study was conventional adenocarcinoma

Age distribution (years)	n (%)
<40	6 (15.00)
41-50	8 (20.00)
51-60	10 (25.00)
61-70	12 (30.00)
>70	4 (10.00)

[Table/Fig-1]: Age-wise distribution of lower gastrointestinal tumours.

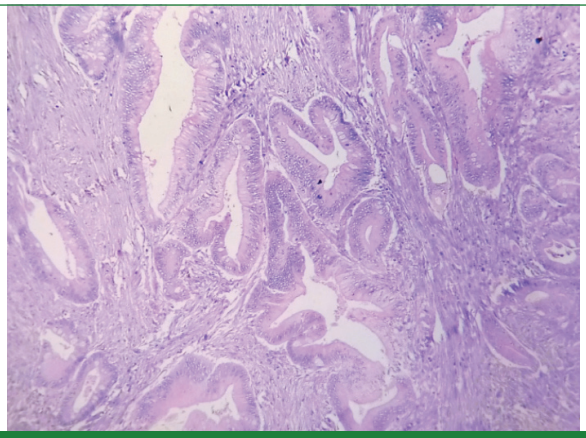
[Table/Fig-2]: Ulcero proliferative growth- colon.



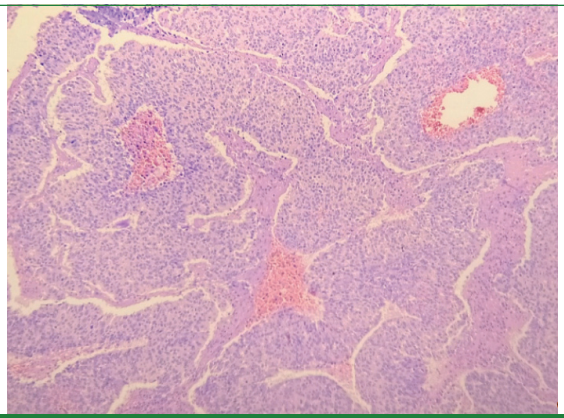
[Table/Fig-3]: Rectosigmoid growth- Abdomino perineal resection (APR) specimen.

of the colon, accounting for 34 (85.0%) cases, followed by mucinous adenocarcinoma in 4 (10.0%) cases, and one case each of papillary adenocarcinoma and squamous cell carcinoma (2.50% each). Tumours were also graded, with 9 (22.50%) cases found to be well differentiated, 30 (75.00%) cases moderately differentiated, and 1 (2.50%) case poorly differentiated [Table/Fig-5-8].

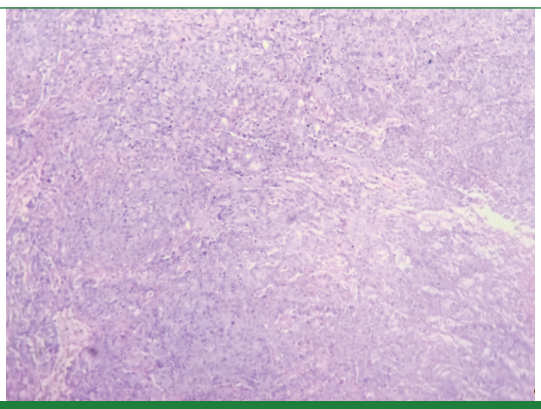
[Table/Fig-4]: Diffuse infiltrative growth with nodal metastasis- colon.



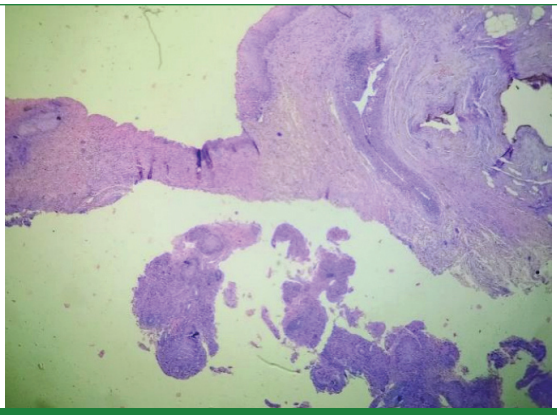
[Table/Fig-5]: Well differentiated adenocarcinoma- colon (H&E, 40x).



[Table/Fig-6]: Moderately differentiated adenocarcinoma- colon (H&E, 40x).



[Table/Fig-7]: Poorly differentiated adenocarcinoma- colon (H&E, 10x).

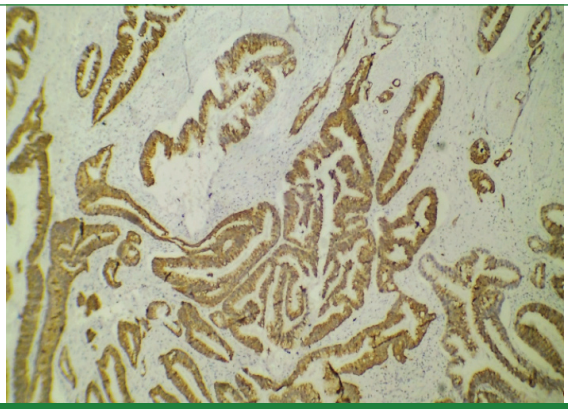


[Table/Fig-8]: Poorly differentiated squamous cell carcinoma- anal region (H&E, 10x).

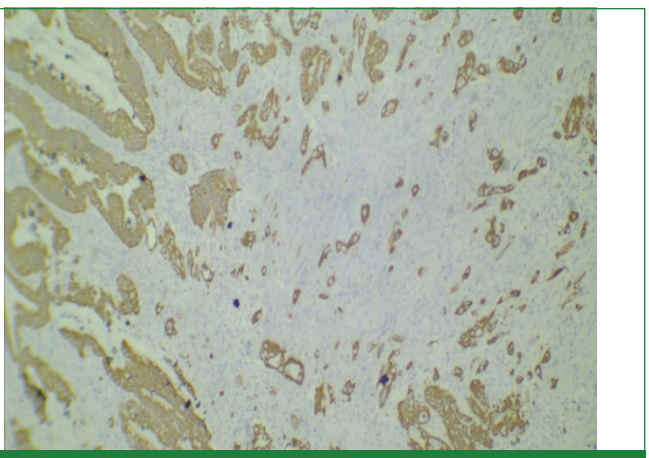
CDH17 expression [Table/Fig-9] in the study sample showed that 38 cases had positive staining. Based on staining intensity, they were categorised as strong (33 cases), moderate (4 cases), weak (1 case), and negative (2 cases) [Table/Fig-10-13]. Immunohistochemical expression of CK7 showed negative staining in about 38 cases, while only two cases showed weak positivity [Table/Fig-9,14-16]. Immunohistochemical staining of CK20 among the study sample showed 37 cases with positive expression for CK20. According to grade moderately differentiated cases were the most numerous (30 cases) [Table/Fig-17]. Based on staining intensity, the results were divided into strong positive (32 cases), moderate positive (4 cases), weak positive (1 case), and three cases that showed CK20 negative expression [Table/Fig-18-21].

Staining intensity	CDH17	CK20	CK7
Strong positive	33 (82.50)	32 (80.00)	0
Moderate positive	4 (10.00)	4 (10.00)	0
Weak positive	1 (2.50)	1 (2.50)	2 (5.00)
Negative	2 (5.00)	3 (7.50)	38 (95.00)

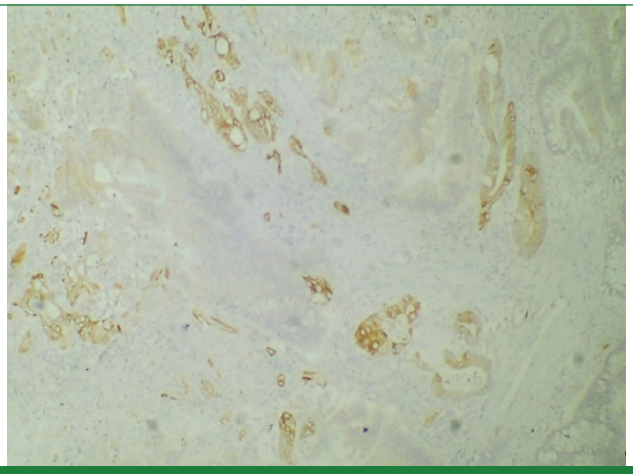
[Table/Fig-9]: Expression of CDH17, CK 20 and CK7 immunohistochemical marker.



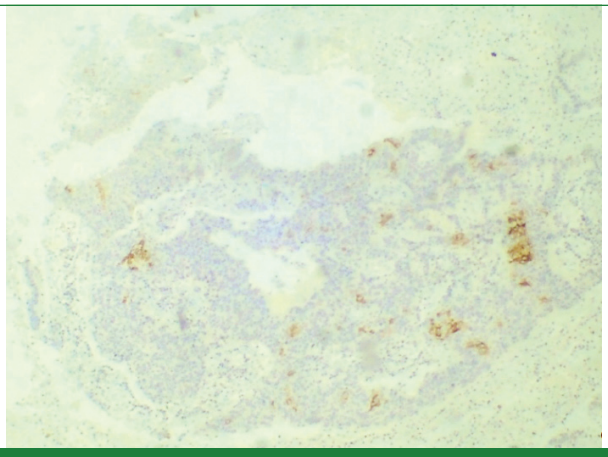
[Table/Fig-10]: CDH17 Expression-score (4+(IHC,4x).



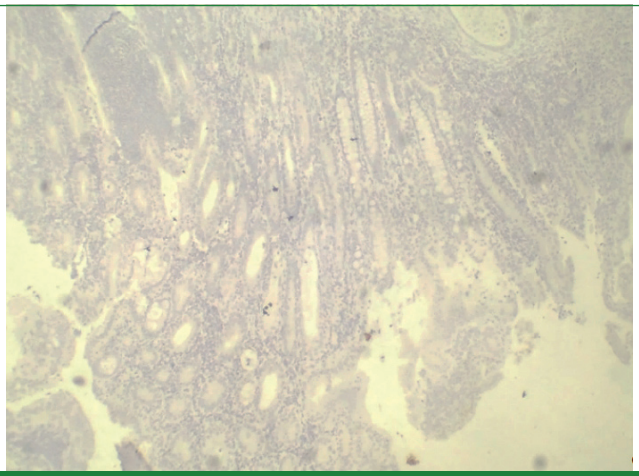
[Table/Fig-11]: CDH17 Expression-score (3+(IHC,4x).



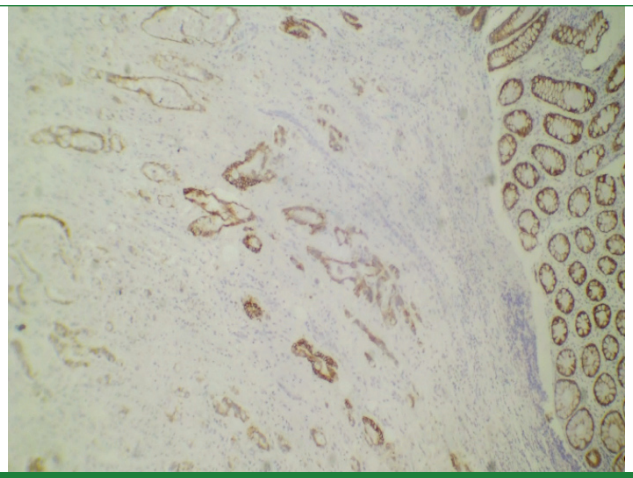
[Table/Fig-12]: CDH17 Expression-score (2+(IHC,4x).



[Table/Fig-13]: CDH17 Expression-score (1+(IHC,4x).



[Table/Fig-14]: CK7 expression-negative (IHC,4x).



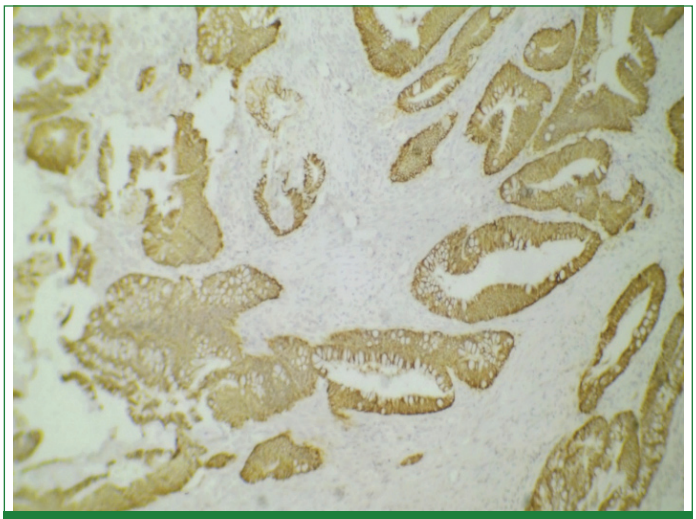
[Table/Fig-15]: CK7 expression- postive (IHC,4x).

Markers	Positive	Negative
CDH17	38	2
CK20	37	3
CK7	2	38

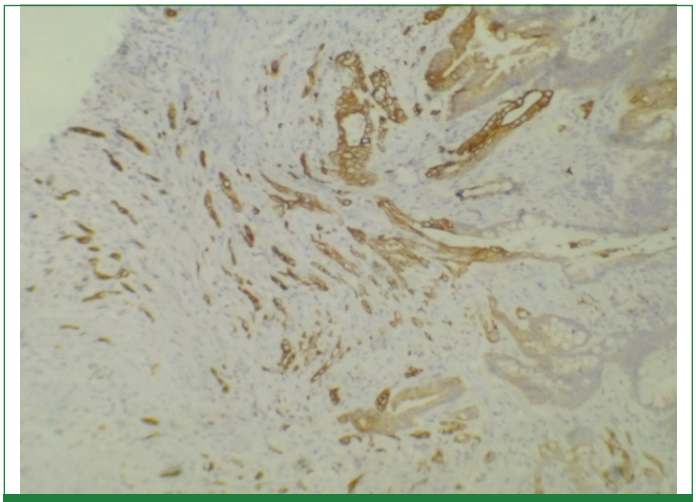
[Table/Fig-16]: Overall expression of immunohistochemical markers.

HPE grade	n (%)
Well differentiated	9 (22.5)
Moderately differentiated	30 (75)
Poorly differentiated	1 (2.5)

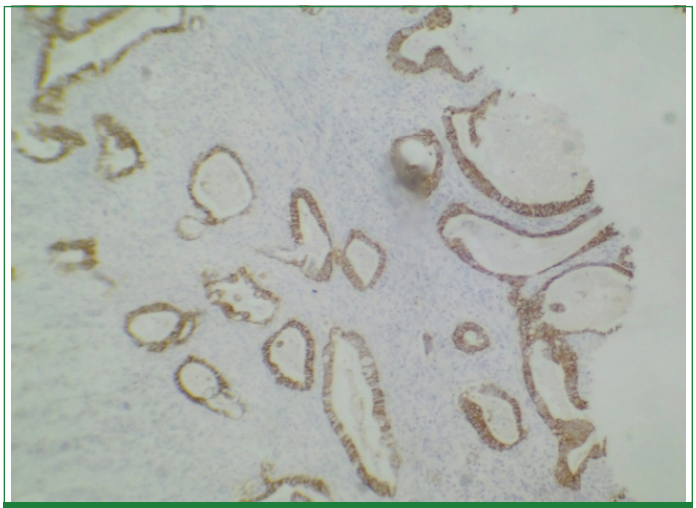
[Table/Fig-17]: Histopathological grade.



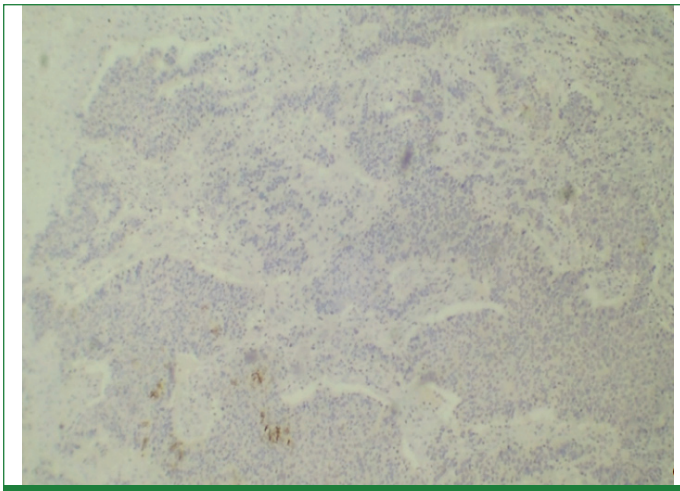
[Table/Fig-18]: CK20 Expression: Score (4+(IHC,4x).



[Table/Fig-19]: CK20 Expression: Score (3+(IHC,4x).



[Table/Fig-20]: CK20 Expression: Score (2+(IHC,4x).



[Table/Fig-21]: CK20 Expression: Score (1+(IHC,4x).

From [Table/Fig-22], four patterns of IHC staining were observed in this study. The most common pattern of IHC expression observed in lower gastrointestinal tract tumours was CDH17 positive/CK20 positive/CK7 negative. About 87.5% of cases showed combined positivity for CDH17 and CK20. The expression of both CDH17 and CK20 markers was more prevalent in the colon and rectal regions compared to the caecum and hepatic flexure, which showed expression of CDH17 and CK20 in only a few cases, as depicted in [Table/Fig-23].

Markers	n (%)
CDH17-ve/CK20-ve/CK7-ve	2 (50)
CDH17+ve/CK20+ve/CK7+ve	2 (50)
CDH17+ve/CK20-ve/CK7-ve	1 (2.5)
CDH17+ve/CK20+ve/CK7-ve	35 (87.5)

[Table/Fig-22]: Panel of markers and their expression.

Site of lesion	Markers			
	CDH17-ve CK20-ve CK7-ve	CDH17+ve CK20+ve CK7+ve	CDH17+ve CK20-ve CK7-ve	CDH17+ve CK20+ve CK7-ve
Rectum	1	0	0	19
Colon	0	2	0	13
Ceacum	0	0	1	2
Hepatic flexure	1	0	0	1

[Table/Fig-23]: Site of lesion vs IHC markers.
Kruskal-Wallis test; p-value-0.003; Significant

Among the various types of lower gastrointestinal tract tumours, such as conventional adenocarcinoma, mucinous adenocarcinoma, papillary adenocarcinoma, and squamous cell carcinoma, We could appreciate that the panel of CDH17 positive/CK20 positive/CK7 negative expression was more towards the conventional adenocarcinoma of the lower GI tumours. The grading of adenocarcinoma in this study showed a high positivity for CDH17 positive/CK20 positive/CK7 negative expression in moderately differentiated adenocarcinoma, with a significance of p-value=0.017 noted through the Kruskal-Wallis test [Table/Fig-24, 25].

HPE diagnosis	Markers			
	CDH17-ve CK20-ve CK7-ve	CDH17+ve CK20+ve CK7+ve	CDH17+ve CK20-ve CK7-ve	CDH17+ve CK20+ve CK7-ve
ADENO CA	1	2	1	30
Mucinous CA	0	0	0	4
Papillary CA	0	0	0	1
Squamous cell CA	1	0	0	0

[Table/Fig-24]: Type of tumourvs IHC markers.
Kruskal-Wallis test; p value -0.017; Significant

HPE grade	Markers			
	CDH17-ve CK20-ve CK7-ve	CDH17+ve CK20+ve CK7+ve	CDH17+ve CK20-ve CK7-ve	CDH17+ve CK20+ve CK7-ve
Well differentiated	0	2	0	7
Moderatley differentiated	1	0	1	28
Poorly differentiated	1	0	0	0

[Table/Fig-25]: HPE grade vs IHC markers.
Kruskal-Wallis test; p-value-0.017; Significant

DISCUSSION

Lower gastrointestinal malignancies have increased in incidence now-a-days due to lifestyle modifications and genetic predisposition. The development of these malignancies is seen among wide range of age groups, but they are more common in individuals aged 50 to 60 years. In this study, the most common age group was the 6th to 7th decade, constituting about 12 cases (30% of the total). Das C et al., found that the most common age group for large intestinal malignancies was 60-70 years [19]. Furthermore, a study conducted by Parikh BJ and Parikh SB, stated that the peak incidence of gastrointestinal malignancies occurs around the sixth decade [20]. Among the 40 cases of lower gastrointestinal malignancies, 25 cases were in males and 15 cases in females. Male preponderance was also seen in other studies conducted by Praveen K et al., [21]. This clearly indicates that the incidence of gastrointestinal tract malignancies is higher in males compared to females, which may be due to the fact that males are exposed to more risk factors.

In this study, out of 40 cases, 19 cases (47.5%) were from the rectum, one from the anus, 15 cases (37.5%) were from the ascending colon, three cases were in the caecum (2.50%), and two cases were in the hepatic flexure (5.00%). Phipps AI et al., found in their study of 3,284 cases of colorectal carcinoma that 24% of cases were located in the rectum, making it the most common site of occurrence of colorectal carcinoma [22]. This observation correlates well with the findings of this study.

Out of the 40 cases in present study, 34 cases were found to be conventional adenocarcinoma (85%), four cases were mucinous adenocarcinoma (10%), one case was papillary adenocarcinoma, and one case was squamous cell carcinoma (2.50%). Most colorectal carcinomas were adenocarcinomas, which correlates well with the study conducted by Wu Y et al., which stated that more than 90% of colorectal carcinomas are adenocarcinomas [23]. The studies by Hajmanoochehri F et al., and Gill MK et al., also reported that the majority of cases included conventional types of adenocarcinoma, which also corresponds well with present study [24,25].

Of the 39 cases of adenocarcinoma, nine cases were well-differentiated (22.50%), 30 cases were moderately differentiated (75.00%), and one case was poorly differentiated (2.50%). Moderately differentiated adenocarcinoma was the most common histopathological grade observed in this study. Sen A et al., also observed moderately differentiated adenocarcinoma was the most common histopathological grade in their study, which was similar to present study findings [26].

The immunohistochemical analysis showed that CDH17 was expressed in colon mucosa, small intestine mucosa, appendix, and pancreatic ducts, but not in acinar cells or islets. CK20 was not found in normal pancreatic ducts but was expressed in the colon, small intestine, appendix, and stomach. CK7 is highly confined to the upper gastrointestinal tract, lungs, and ovaries. Present study examined 38 cases of lower gastrointestinal malignancies, mostly from the colorectum, which showed positive staining for CDH17. Based on the staining intensity, the cases were categorised as follows: strong (33 cases, 82.50%), moderate (four cases, 10%), weak (one case, 2.50%), and negative (two cases, respectively). The CK7 staining characteristics in present study population included two weak positive cases (5%) and 38 negative cases (95%). The

expression of CK20 in this study population was as follows: 32 strong positive cases (80.00%), four moderate positive cases (10.00%), one weak positive case (2.50%), and three negative cases (7.50%).

Yantiss RK et al., study states that CDH17 immunostaining was positive in 97.3% (145 of 149) of colon adenocarcinomas, whereas CK20 stained positively in 88.6% (132 of 149) of cases [27]. They also suggested that CDH17 stained 100% (99/99) of colon adenocarcinomas, whereas CK20 and CDX2 stained 92% (91/99) and 96% (95/99), respectively. In mucinous adenocarcinomas, CDH17 and CK20 stained 80% (4/5) and CDX2 stained 60% (3/5). Connelly JH et al., stated that colorectal adenocarcinomas showed staining in 96% of cases, with most showing strong and diffuse staining. Both studies corresponds well with present study [28].

In this study, four patterns of CDH17/CK7/CK20 expression were observed. The most common pattern in lower gastrointestinal tract tumours was CDH17 positive/CK20 positive/CK7 negative. About 87.5% of cases showed combined positivity for CDH17 and CK20, while CDH17 negative/CK20 negative/CK7 negative was observed in two cases (5%). The pattern of CDH17 positive/CK20 positive/CK7 positive was seen in two cases (5%), and CDH17 positive/CK20 negative/CK7 negative was observed in one case (2.50%). Connelly JH et al., also compared the cadherin-17/cytokeratin 7 profile expression, out of which 37 of 38 (97%) cadherin-17 positive/cytokeratin 7 negative tumours were colorectal adenocarcinomas, indicating that cadherin-17 is a useful immunohistochemical marker for diagnosing adenocarcinomas of the colorectum [28].

Goldstein NS et al., helped clarify that CK20 was expressed in a higher percentage of colorectal cancers [29]. They identified four patterns of CK20/CK7 expression: CK20 positive/CK7 negative (60.4%), CK20 positive/CK7 positive (2.1%), CK20 negative/CK7 negative (35.4%), and CK20 negative/CK7 positive (2.1%). Non neoplastic colonic mucosa proximal to the rectum exhibited a CK7 negative/CK20 positive phenotype, as do 90% of colorectal cancer. Both studies are concordant with present study expression. Kende AI et al., studied the IHC expression of CK7 and CK20 in lesions from 105 patients, showed well-differentiated and moderately differentiated adenocarcinomas of the large intestine, including the appendix, predominantly showed a CK7 negative/CK20 positive pattern [30]. Ordóñez NG, reported that adenocarcinomas arising in the gastrointestinal tract expressed cadherin 17 in the vast majority of both primary (96% to 100%) and metastatic carcinoma cases [31,32]. In a combined review of six large published series on the expression of the CDH17 marker in primary gastrointestinal adenocarcinomas, 329 (99%) of 333 cases of colon cancer, 247 (44%) of 565 cases of stomach cancer, and 51 (75%) of 68 cases of esophageal cancer were found to be cadherin 17 positive. This series of studies clearly states that CDH17 is more specific for colon malignancies. Panarelli NC et al., evaluated CDH17 as a diagnostic marker for gastrointestinal carcinomas, particularly those with intestinal differentiation, and compared its usefulness with that of CDX2 [33]. Present study found concordant staining of both markers in most colonic, oesophageal, and gastric adenocarcinomas (99%, 79%, and 86%, respectively). Colonic carcinoma stained nearly 99%, which was comparable to present study. The prognostic effects of CDH17 were investigated by Park SS et al., on 208 paired gastric endoscopic biopsy and resection specimens that contained adenocarcinoma. They found that weak or absent CDH17 staining in biopsy samples predicted the presence of lymph node metastases in resection specimens [34]. Other authors have stated that the lack of CDH17 staining is associated with a better prognosis. Preliminary studies also suggest that CDH17 immunoexpression may have prognostic implications for patients with colorectal cancer. Yanagisawa Y et al., compared 207 colorectal carcinomas with non neoplastic colonic epithelium and found that tumours with reduced CDH17 labeling were associated with a better prognosis [35]. Al Maghrabi J et al., showed that the CK20+/CK7– profile is expressed in about 75-95% of colorectal cancers, while the rest of the cases show different profiles [17]. Occasionally, loss of CK20 expression and conversely positive expression of CK7 were noted in some colorectal cancer. The value of this aberrant expression is still unclear [36]. In primary colorectal cancer, CK20 was positive in 62.5%, while CK7 was positive in 5.6%. In nodal metastases, CK20 and CK7 showed positivity in 63.5% and 4.1%, respectively. The reason behind the unusual immunostaining of CK20 and CK7 is still unclear. Recent molecular studies categorised colorectal cancer into microsatellite stable and microsatellite unstable tumours. Other studies examined CK20/CK7 expression in 44 colorectal cancer cases in relation to molecular subtypes and concluded that reduction or total absence of CK20 is a phenotypic characteristic of colorectal cancer originating through Microsatellite Instability (MSI). On the other hand, Gurzu S and Jung I stated that microsatellite instability colorectal cancer are associated with diffuse expression of CK7 and absence of CK20 [37]. The above results can explain the aberrant expression of CK20 and CK7 in a percentage of colorectal cancer, which is comparable to our study. Bressenot A and Zimmer O suggested that aberrant expression of CK20 and CK7 is related to tumour progression, based on one of their cases [38].

Limitation(s)

More cases of malignancies from the caecum and hepatic flexure were not assessed due to a limitation in the specimens received.

CONCLUSION(S)

Lower gastrointestinal malignancies have been on the rise in recent years, in addition to various epidemiological factors. New IHC markers are emerging and being widely used. IHC markers give us an excellent insight into the molecular basis of cancer evolution, which aids clinicians and oncologists in the targeted therapy of tumours. Present study documented the expression of CDH17 and CK20 in lower gastrointestinal malignancies, particularly in colorectal cancer, where the expression was found to be strong and diffuse. CDH17 expression correlated with the site of the lesion, as well as with the grading and differentiation of colorectal malignancies, which was statistically significant. Increased expression of CDH17 and CK20 was seen in moderately differentiated and decreased expression is seen in poorly differentiated colorectal carcinomas. In contrast, the CK7 marker was not expressed in lower gastrointestinal malignancies, indicating a negative correlated in present study. Thus, the IHC markers CDH17 and CK20 can be routinely employed as cocktail markers in lower gastrointestinal malignancies.

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