

CLINICO-HISTOPATHOLOGICAL ANALYSIS OF PRE-MALIGNANT AND MALIGNANT LESIONS OF THE INTESTINAL TRACTHARITHA BELLAPU¹, ANURADHA B², SUJATHA C², SHAHANUMA SHAIK^{2*}¹Department of Pathology, Sri Devaraj Urs Medical College, Kolar, Karnataka, India. ²Department of Pathology, S. V. Medical College, Tirupati, Andhra Pradesh, India. Email: shahanuma@gmail.com

Received: 28 April 2023, Revised and Accepted: 13 June 2023

ABSTRACT**Objective:** The current study's aim is to correlate clinical variables with histopathological findings of pre-malignant and malignant lesions of the intestinal tract.**Methods:** The sample size includes all the endoscopic biopsies and surgically resected specimens of the intestinal tract received at the Department of Pathology, S.V. Medical College, Tirupati for 2 years from November 2016 to October 2018. All the specimens are fixed in 10% formalin and stained with Hematoxylin and Eosin. Special stains and Immunohistochemistry were done wherever required.**Results:** During the study, we studied 113 specimens of endoscopic biopsies and 759 specimens of surgically resected. Out of 113 endoscopic biopsies, 33 biopsies were premalignant and malignant lesions, among which 8 were premalignant lesions and 25 were malignant. Out of 759 surgically resected specimens, 37 specimens were premalignant and malignant lesions, among which 1 was premalignant and 36 were malignant. Out of 70 lesions, 3 occurred in the small intestine, 59 occurred in large intestine, 8 occurred in the anal canal. In the small intestine, 3 lesions were encountered among which, one each of adenoma, PJP, adenocarcinoma was noted. Out of 59 lesions of large intestine 4 were adenomas, 2 were ulcerative colitis, 48 were adenocarcinoma and its variants, 2 were MANECs, one each of carcinoid and GIST and malignant melanoma were reported. In the anal canal, there were 1 adenoma, 2 mucinous adenocarcinomas, and 5 squamous cell carcinomas reported. A case of adenoma occurred in male patient, among 2 mucinous adenocarcinomas one occurred in female patient and one in male patient. Out of 5 squamous cell carcinomas, 3 occurred in female patients and 2 in male patients. Among 3 lesions of the small intestine, one case each of adenoma, PJP, and adenocarcinoma, all occurred in male patients. 33 out of 48 adenocarcinomas occurred in male patients. The most common symptom was bleeding per rectum (63.83%) followed by constipation, pain in abdomen and diarrhea. The association between Adenocarcinoma and Smoking is not correlated with $p=0.67$. The association between Adenocarcinoma and Smoking is not correlated with a $p=0.38$.**Conclusion:** Most of the neoplasms were from the large intestine followed by the anal canal. The most common neoplasm and also most common malignancy was Adenocarcinoma. Different variants of adenocarcinoma encountered in the study were Mucinous adenocarcinoma and Signet ring cell adenocarcinoma. Adenomas were common in Male patients. Mixed adenoneuroendocrine tumor and gastrointestinal stromal tumor of large intestine were confirmed with IHC study.**Keywords:** Hematoxylin and eosin, Adenocarcinoma, Large intestine, GIST, Mucinous adenocarcinoma.© 2023 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2023v16i7.48622>. Journal homepage: <https://innovareacademics.in/journals/index.php/ajpcr>**INTRODUCTION**

The small intestine and colon make up a large part of the gastrointestinal tract and are the sites of a broad array of diseases. Colorectal cancer (CRC) is a major cause of morbidity and mortality throughout the world [1]. Prevention is based on early endoscopic detection of potentially curable cancers or precursor conditions such as dysplasia, which have a significant risk of progression to malignancy [2]. The small intestine represents the longest part of the digestive tract, making up 75% of the length [3]. Malignant tumors of the small intestine are very rare, compared to other gastrointestinal organs [4], with a global incidence of <1.0/100000 population [3]. An increased risk has been noted for individuals with Crohn disease, celiac disease, adenoma, familial adenomatous polyposis, and Peutz-Jeghers syndrome (PJS). The most common malignant tumors are carcinoid and adenocarcinoma, followed in order by gastrointestinal stromal tumor and malignant lymphoma.

Primary appendiceal cancer is diagnosed in 0.9–1.4% of appendectomy specimens. These rare tumors are seldom suspected before surgery and less than one-half of the cases are diagnosed intraoperatively [5]. The age-adjusted incidence of cancer of the appendix was 0.12 cases per 1,000,000 people per year.

CRC is the third most commonly diagnosed malignancy and the fourth leading cause of cancer death in the world [6]. CRC incidence peaks

between the age of 60 and 70 years, while its occurrence in patients below 40 years is rare. CRC develops from the progression of acquired or hereditary premalignant lesions [7]. Although most colorectal adenomas are benign lesions, a small proportion may harbor invasive cancer at the time of detection. Dysplasia and malignant transformation represent the most important complication in patients with inflammatory bowel disease.

Anal cancer is uncommon, with incidence rates mostly between 1 and 2/100 000 per year. Squamous cell carcinoma and its variants account for about 70% of all anal cancers high-risk human papillomavirus types can be detected in 80–90% of all anal SCC cases [8].

Endoscopy has become the most commonly performed procedure in the detection of premalignant and malignant lesions of GI tract. Endoscopy is a visual examination of the gastrointestinal tract using a lighted flexible fiber optic or video endoscope. These lesions are diagnosed by endoscopy in combination with biopsy. Histopathological examination of resected specimens will aid in confirmatory diagnosis, type of tumor staging and grading of tumor, and predicting the prognosis after surgical resection.

METHODS**Source of data**

Data are collected from patients and Hospital Records of patients presented with lesions in the intestinal tract in the Department of

Surgery, S.V.R.R.G.G.H, Tirupathi with their respective biopsies sent to the Department of Pathology, S. V. Medical College, Tirupathi, for further evaluation.

The sample size includes all the endoscopic biopsies and surgically resected specimens of the intestinal tract received at Department of Pathology, S.V. Medical College, Tirupathi.

Method of collection of data

All the endoscopic biopsies and surgically resected specimens of intestinal tract received in the department of pathology are fixed in 10% formalin and routinely processed. 3–5 micron thick sections will be made from paraffin-embedded blocks and stained with Hematoxylin and Eosin. Special stains and Immunohistochemistry are done wherever required. A detailed study of the section will be done under the microscope.

Study design and duration

The present study is a Cross-sectional study for 2 years from November 2016 to October 2018.

Inclusion criteria

Biopsies and resected specimens of the intestinal tract were diagnosed as premalignant and malignant lesions by histopathological examination patients who have consented to the study.

Exclusion criteria

Inadequate samples and samples not properly fixed and Samples with extensive tumor necrosis.

Methodology

Data for the study were taken from all those who fulfilled the inclusion criteria on purposive sampling. Brief clinical data were noted from the case records, which included the age and sex of the patients, relevant habits if any, presenting symptoms, endoscopic findings, and diagnosis. The lesions were diagnosed as per the WHO classification of tumors in 2010.

Statistical analysis

The clinical and histological data so obtained were analyzed using SPSS Statistics version 23 software and the results are depicted in the form of graphs and charts.

RESULTS

From November 2016 to October 2018, we studied 872 specimens regarding the intestinal tract. Among these 872 specimens, 113 specimens were endoscopic biopsies and 759 specimens were surgically resected specimens. Out of 113 endoscopic biopsies, 33 biopsies were premalignant and malignant lesions, among which 8 were premalignant lesions and 25 were malignant. Out of 759 surgically resected specimens, 37 specimens were premalignant and malignant lesions, among which 1 was premalignant and 36 were malignant.

Out of 70 lesions, 3 occurred in the small intestine (Duodenum, Jejunum, and Ileum), 59 occurred in large intestine (Cecum, Colon, and Rectum), 8 occurred in the Anal canal (Table 1).

In the small intestine, 3 lesions were encountered among which, one each of adenoma, PJP, adenocarcinoma was noted. Out of 59 lesions of large intestine 4 were adenomas, 2 were of ulcerative colitis, 48 were adenocarcinoma and its variants, 2 were MANECs, one each of carcinoid and GIST and malignant melanoma were reported. In the anal canal, there were 1 adenoma, 2 mucinous adenocarcinomas, and 5 squamous cell carcinomas reported (Figure 1).

Age

Out of 3 small intestinal lesions (Duodenum - 1, Jejunum - 1 and Ileum - 1), one adenoma occurred >70 years of age, 1 case of PJP occurred <30 years of age and 1 adenocarcinoma occurred >50 years of age (Table 2).

Out of 59 premalignant and malignant lesions of large intestine (Cecum - 5, Colon -22 and Rectum - 32), out of 4 adenomas 3 cases occurred after 50 years of age and 31 out of 48 adenocarcinomas occurred after 50 years of age.

Age-wise incidence of premalignant and malignant lesions of the anal canal

1 case of adenoma occurred in 50 years age group. Out of 7 malignancies of anal canal, 2 cases of mucinous adenocarcinoma, 5 cases of squamous cell carcinoma occurred after 50 years of age.

Sex-wise incidence of premalignant and malignant lesions of anal canal

A case of adenoma occurred in male patient, among 2 mucinous adenocarcinomas one occurred in female patient and one in male patient. Out of 5 squamous cell carcinomas, 3 occurred in female patients and 2 in male patients.

Among 3 lesions of the small intestine, one case each of adenoma, PJP, and adenocarcinoma, all occurred in male patients.

Among 59 lesions of large intestine, 2 adenomas occurred in male patients and 2 in female patients. 33 out of 48 adenocarcinomas occurred in male patients.

Association of smoking with lesions

Out of 62 premalignant and malignant lesions of the intestinal tract smoking habit was present in 14 cases. Out of 3 cases of small intestine 2 patients were smokers. 12 out of 41 male patients with large intestinal lesions were smokers.

Association of alcoholism with lesions

Out of 62 premalignant and malignant lesions of intestinal tract 27 cases were known Alcoholics. Two out of 3 male patients with small intestinal lesions were alcoholics. 22 out of 41 male patients, 3 out of 18 female patients with large intestinal lesions were alcoholic.

For most of the adenomas, 5 out of 6 presented with Bleeding per rectum. Most of the adenocarcinomas presented with bleeding per rectum followed by Pain abdomen. All the anal canal malignancies presented with Bleeding per Rectum followed by constipation (Table 3).

DISCUSSION

Premalignant and malignant lesions of the intestines including the anal canal were analyzed in the present cross-sectional study for 2 years. Features such as site-wise distribution, age and sex-wise distribution, correlation with the presenting clinical symptoms, and association with smoking and alcoholism were studied. Premalignant conditions of the small intestine such as Crohn's disease, PJS are associated with significant morbidity and considerable predisposition to malignancy [9]. Neoplastic polyps of the colorectum, namely tubular and villous adenomas, are precursor lesions of colorectal cancer. Inflammatory bowel diseases, ulcerative colitis, and Crohn's disease increase an individual's overall risk of developing colorectal cancer [10]. Both colorectal premalignant and overt malignant lesions are usually asymptomatic and their development is highly insidious. Consequently, screening is often necessary to detect preneoplastic lesions and CRC in its early stages [7].

The specimens included endoscopic biopsies and surgically resected specimens of the intestinal tract and anal canal. A total of 872 specimens of intestinal tract 464 (53.2%) specimens were from the appendix. 13% of all specimens were Endoscopic biopsies and the rest were surgically resected specimens.

In the present study, malignant lesions were more common than premalignant lesions. Most of the malignancies occurred in the large intestine (86.8%) followed by anal canal (11.5%). These findings are in concordance with the study of Sulegaon *et al.* [11] whereas in study

Table 1: Spectrum of premalignant and malignant lesions in different parts of the intestinal tract

Diagnosis	Small intestine			Large intestine			Anus	Total
	Duodenum	Jejunum	Ileum	Cecum	Colon	Rectum		
Pre-malignant								
Adenoma	1	--	--	--	1	3	1	6
PJS	--	1	--	--	--	--	--	1
UC	--	--	--	--	1	1	--	2
Malignant								
WDAC	--	--	1	2	11	13	--	27
MDAC	--	--	--	--	5	9	--	14
PDAC	--	--	--	--	--	1	--	1
MAC	--	--	--	2	1	3	2	8
SRAC	--	--	--	--	--	1	--	1
MANEC	--	--	--	--	2	--	--	2
NET	--	--	--	--	1	--	--	1
GIST	--	--	--	1	--	--	--	1
WDSCC	--	--	--	--	--	--	1	1
MDSCC	--	--	--	--	--	--	4	4
MM	--	--	--	--	--	1	--	1
Total	1	1	1	5	22	32	8	70

PJS: Peutz-Jeghers syndrome

Table 2: Age-wise incidence of pre-malignant and malignant lesions of the large intestine

Age	Adenoma	UC	AC	MANEC	NET	GIST	MM	Total (%)
<20	--	--	--	--	--	--	--	--
21-30	--	--	1	--	--	--	--	1 (1.7)
31-40	1	--	3	--	--	--	--	4 (6.8)
41-50	--	2	13	2	1	1	--	19 (32.2)
51-60	1	--	16	--	--	--	1	18 (30.5)
61-70	2	--	11	--	--	--	--	13 (22)
71-80	--	--	4	--	--	--	--	4 (6.8)

Table 3: Correlation of pre-malignant and malignant lesions with clinical features

	Bleeding per rectum	Constipation	Pain abdomen	Diarrhea
Adenoma	5	1	1	1
PJS	--	--	1	--
UC	2	--	1	2
WDAC	19	7	16	3
MDAC	12	9	11	1
PDAC	1	--	1	--
MAC	5	5	5	1
SRAC	--	1	1	--
MANEC	1	--	2	1
NET	--	--	1	1
GIST	--	1	1	--
WDSCC	1	--	--	--
MDSCC	4	2	--	--
MM	1	--	--	--
Total (%)	51 (72.8%)	26 (37.1%)	41 (58.5%)	10 (14.2%)

PJS: Peutz-Jeghers syndrome

by Singh *et al.*, [12] most of the malignancies are in the large intestine followed by small intestine.

In the present study, adenocarcinoma and its variants were the most common malignancies among the small and large intestines accounts 83.6%, followed by Squamous cell carcinoma (8.2%) and the rest includes MANECs, GIST, MM, and NET.

In comparison with Sulegaon *et al.*, in the present study, the most common malignancy is adenocarcinoma and followed by squamous

cell carcinoma. Two cases of MANEC were reported in the present study. One each of Carcinoid, GIST, and malignant melanoma were reported.

Gastrointestinal stromal tumors are mesenchymal tumors of the Gastrointestinal tract with unequivocal immunohistochemical C-kit positivity. They arise from the interstitial cells of Cajal and they account for 0.1-3% of all G.I malignancies [13].

In the present study, 1 case of GIST occurred in the cecum, presented with pain abdomen and constipation. On immunohistochemistry showed strong and diffuse cytoplasmic positivity with C-kit (CD117) and membranous and cytoplasmic positivity with DOG-1.

Two cases of MANEC cases reported in the present study. On immunohistochemistry, one case showed positivity with CK-20, NSE and showed negativity with Ck-7 and Chromogranin.

Malignant melanoma of the rectum is an extremely rare disease. It typically presents in the fifth or sixth decade of life with nonspecific complaints such as rectal bleeding or anal pain [14,15]. One case of malignant melanoma occurred in Rectum in a 60-year-old male patient, who presented with bleeding per rectum.

Lesions of the small intestine

In the present study, there were 2 cases of premalignant lesions and one case of malignant lesions.

Premalignant lesions

Adenoma: one case of adenoma occurred in the duodenum (33.3%) in a 74-year-old male patient.

PJS: one case of PJS occurred in the jejunum in 25 years male patient.

Malignant lesions

Adenocarcinoma: one case of well-differentiated adenocarcinoma occurred in 60 years male patient in the ileum.

Lesions of the large intestine

Adenomatous polyp

In the present study, 4 cases of adenomas occurred, one in the colon and 3 in the rectum. All cases presented with bleeding per rectum. On histology, 2 showed a villous pattern, one showed a tubular pattern and the other 1 showed a tubulovillous pattern.

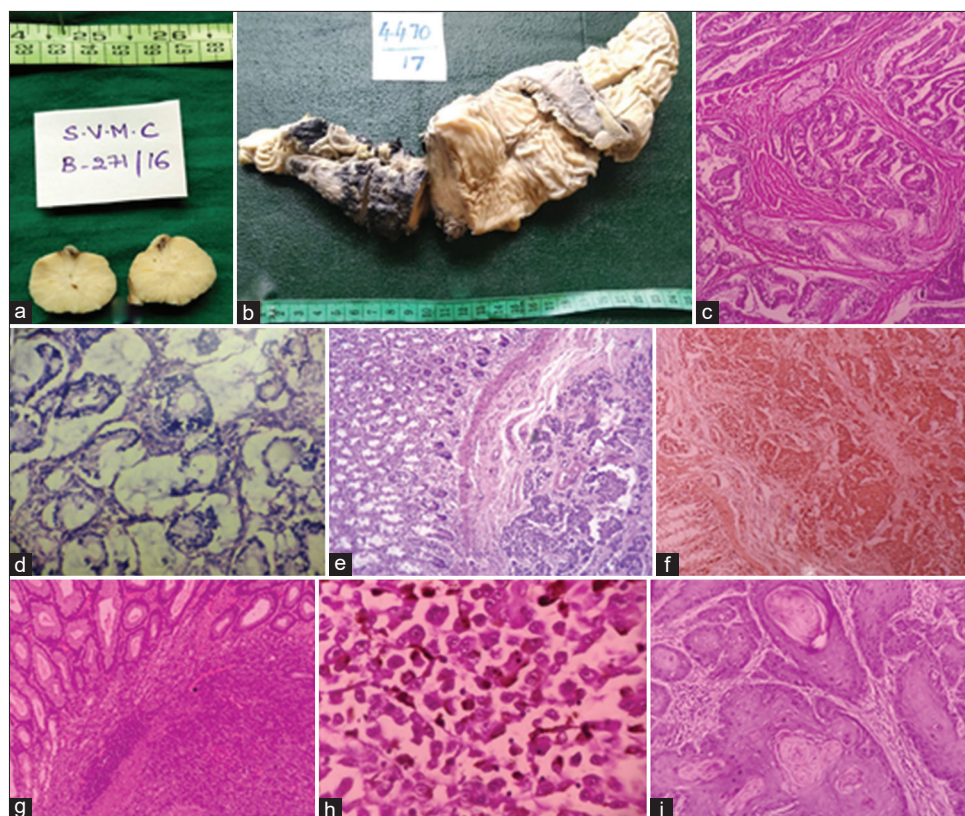


Fig. 1: (a) Peutz-Jeghers polyp. (b) Adenocarcinoma of the colon presents as growth. (c) microphotograph Peutz-Jeghers Polyp ($\times 100$). (d) Microphotograph Mucinous Adenocarcinoma ($\times 10$). (e) Microphotograph mixed adenoneuroendocrine carcinoma ($40\times$). (f) MANEC showing NSE positivity. (g) microphotograph-gastrointestinal stromal tumor ($\times 100$). (h) microphotograph-rectal melanoma ($\times 400$). (i) well-differentiated squamous cell carcinoma anus ($\times 100$)

Ulcerative colitis

In the present study, 2 cases of ulcerative colitis, both in male patients and in the age group of 41–50 occurred.

The mean age of presentation of colonic adenomatous polyps in the present study is 58.6 which is in concordance with the study by Tony *et al.* [16] Both Tony *et al.* study and the present study are showing male predominance.

Sood *et al.*, [17] in their study in Punjab found that the mean age of presentation of ulcerative colitis was 35.32 years with the commonest symptoms being pain in the abdomen and per rectal bleeding. In the present study, the mean age is 45 with the most common presenting symptom being Bleeding per rectum. Mean age for ulcerative colitis is older than studies by Sood *et al.* and Price and Morson [18].

In comparison with Rasool *et al.* [19] study, where a maximum number of malignancies occurred in 51–60 years of age group followed by 41–50 years of age group, the present study is in concordance with the Rasool *et al.*'s study. There were no cases of adenocarcinoma observed in the age group below 20 years and in the age group of 81–90 years in the present study. In the present study minimum age at which Adenocarcinoma occurred is 30 years and the maximum age is 80 years.

In the present study, the mean age of presentation of adenocarcinoma of the large intestine is 56.3 years which is in concordance with Singh *et al.* study, whereas in studies by Rasool *et al.* and Rasool *et al.* [20] the mean age is at a younger age.

The present study is in concordance with the study by Singh *et al.* with respect to sex incidence. Compared to the study by Laishram *et al.*, [21] Rasool *et al.*, Rasool *et al.*, the present study is showing more male predominance.

Comparison of large intestinal malignancies

In comparison with Laishram *et al.* study, in the present study, there is more male preponderance whereas in his study there is slight male preponderance. In both studies, the maximum proportion of large intestinal malignancies occurred in Rectum.

Comparison of large intestinal malignancies

In the present study and Karsner's [22] study, the most common age group affected by large intestinal malignancies was more than 50 years and in both studies the major incidence of large intestinal malignancies was in Rectum.

Distribution of histological types of adenocarcinoma of large intestine

Shah *et al.*, in their study of 107 cases of colorectal carcinoma found that 72% of the cases were of well-differentiated type while mucinous adenocarcinoma constituted 20% of the cases. In the present study, well-differentiated adenocarcinoma constituted about 52.95%, moderately differentiated type 27.45%, and mucinous type about 15.68% of cases. Poorly differentiated adenocarcinoma and Signet ring adenocarcinoma constituted only 1.96% of each. Sulegaon *et al.* and Caliskan *et al.* [23] in their study found moderately differentiated adenocarcinoma as the most common type.

Symptoms

In a study by Sulegaon *et al.*, 68 cases of malignant lesions were seen in the large intestine. The most common symptom was bleeding per rectum (63.83%) followed by constipation, pain in abdomen, and diarrhea.

In the present study, 53 cases of malignant lesions occurred in the large intestine. The most common symptom was pain abdomen (69.8%) followed by bleeding per Rectum, constipation, and diarrhea. No

pre-malignant and malignant lesions occurred in the appendix in the present study.

Comparison of anal canal malignancies

In comparison with Johnson *et al.* [24] and Klas *et al.* studies, in all the studies Squamous cell carcinoma was the most common malignancy of the anal canal. In all the studies mentioned above, most of the malignancies occurred after 50 years of age, the mean age was also above 50 years and there is female predominance.

Association of smoking and alcoholism

The association between adenocarcinoma and smoking is not correlated with $p=0.67$. The association between adenocarcinoma and smoking is not correlated with a $p=0.38$.

CONCLUSION

Malignant lesions were more common than pre-malignant lesions. Most of the neoplasms were from the large intestine followed by the anal canal. The most common neoplasm and also most common malignancy was adenocarcinoma. The most common pre-malignant lesion was adenoma. Maximum number of neoplasms occurred in the age group of >50 years. Except in the anal canal, all the intestinal malignancies were more common in male patients. The most common presenting symptom was pain abdomen followed by bleeding per rectum. At the time of presentation, most of the adenocarcinomas were well differentiated. Different variants of adenocarcinoma encountered in my study were acinous adenocarcinoma and Signet ring cell adenocarcinoma. All the adenomas were seen >50 years of age. The proportion of adenomas was highest in the large intestine. Adenomas were common in Male patients. Mixed adenoneuroendocrine tumor and gastrointestinal stromal tumor of the large intestine were confirmed with the IHC study. Endoscopy and endoscopic biopsies were not only diagnostic tools but also very efficient screening tools for gastrointestinal neoplasms.

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