



Clinico-Pathological Spectrum of Colonic Lesions

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Abstract

Background: *The colon is a seat for various diseases which include both non neoplastic and neoplastic conditions. However, due to considerable overlap in clinical manifestations in the colonic lesions further investigations are crucial in determining underlying pathology. With the advent of flexible fibre optic sigmoidoscopy and colonoscopy adequately sampled biopsies facilitate documenting normal colonic mucosa, identifying inflammatory processes, discriminating different inflammatory reaction patterns, suggesting the possibility of more than one disease process and also, at times, identifying a specific causative agent.*

Materials and Methods: *All colonoscopic biopsies received in Department of Pathology in a tertiary care hospital in southern India during the two-year study period.*

Results: *Total of 98 colonoscopic biopsies were studied with a male to female ratio of 2.3: 1. Most common clinical presentation for both benign as well as malignant lesions was bleeding per rectum. Out of the colonoscopic biopsies, 45 (45.9%) were non neoplastic, 8 (8.16%) were benign lesions and 35 (35.78%) were malignant lesions. Among the 45 Non neoplastic lesions, 22 cases (48.8%) were non-specific colitis, 17 (37.7%) cases ulcerative colitis, 3 cases (6.66%) granulomatous inflammation, 2 cases (4.44%) inflammatory polyps and 1 case (2.22%) of juvenile polyp. Out of the 8 benign cases, 4 cases (50%) of tubulovillous adenoma, 3 cases (37.5%) of tubular adenomas, 1 case villous adenoma (12.5%). Out of 35 malignant lesions, 4 cases (11.4%) were Well Differentiated Adenocarcinoma, 24 cases (68.5%) were Moderately Differentiated Adenocarcinoma, 5 cases (14.2%) were Poorly Differentiated Adenocarcinoma, 1 case (2.8%) each of Mucin Secreting Adenocarcinoma and Malignant Melanoma.*

Conclusion: *Though clinical features supplemented with colonoscopy serve as an adequate tool to diagnose colonic pathology, histopathology remains the gold standard for definitive diagnosis.*

Keywords: *Colonoscopy, Colitis, Colorectal carcinoma, IBD, Adenoma.*

Introduction

Numerous acute and chronic inflammatory and neoplastic disorders affect the lower gastrointestinal tract¹ encompassing a spectrum of colonic lesions from infectious, idiopathic, inflammatory diseases, polyps, motility disorders to frank colorectal tumours.²

The colon is also a host to a number of primary and secondary neoplasms, causing a formidable health problem worldwide. Although 60% of cases are encountered in developed countries, India is showing a rising trend.³

There is considerable overlap in clinical manifestation of colonic lesions with patients presenting with abdominal pain, constipation,

diarrhoea, bleeding per rectum and change in bowel habits. Hence, further investigations are crucial in determining underlying pathology.

Colonoscopy - developed in the early 1970 - is central in diagnosing and managing colorectal disorders. With the development of flexible fibre optic sigmoidoscopy and colonoscopy, the clinical management of colorectal diseases has been further revolutionized.⁴ Colonoscopy prevails over other techniques with its simultaneous ability to visually inspect the entire length of the colon (including the distal ileum), allowing sample-tissue collection for histological evaluations as well as undertaking therapeutic intervention by haemostasis, removal of polyps, dilatation of strictures and decompression of the obstructed bowel. It aids in determining prognosis and appropriateness of medical therapies as well as decision making among those undergoing surgical therapy.

Various conditions affecting the colon are diagnosed by collecting mucosal biopsies during colonoscopic evaluation. Histopathological investigation of these biopsies takes into account four main categories like mucosal architecture, lamina propria cellularity, inflammatory cells infiltration and epithelial abnormalities for their conclusive diagnosis.⁵

Biopsies can be sought to evaluate the response to therapy and detecting complications. Mucosal biopsies have been shown to accurately indicate colonic diseases and aid in determining rational therapeutic strategies in the affected population.⁶

In premalignant conditions such as Ulcerative Colitis and Crohn's disease, Colonoscope acts a tool for cancer surveillance and helps in early detection of cancerous lesions.

In some instances, a macroscopically normal colonic mucosa may be pathologically inflamed. Thus, in the absence of biopsies, significant inflammatory bowel disease may go unrecognized or be misdiagnosed for a functional disorder.

Therefore, if the colon is adequately sampled, biopsy samples could facilitate the following:

1) Documenting normal colonic mucosa,⁷

- 2) Identifying inflammatory processes in an endoscopically normal appearing colonic mucosa,⁷
- 3) Identifying and discriminating different inflammatory reactions patterns that reflect pathogenesis and duration,⁷
- 4) Suggesting the possibility of more than one disease process,⁷
- 5) Identifying, at times, a specific causative agent.⁷

Though Colonoscopy comes with undesirable features of being an invasive, need for sedation and analgesia, test risks and patient discomfort, newer developments in colonoscopy are trying to reduce or eliminate these effects.⁸ Virtual Colonoscopy, CT guided Colonoscopy are proving attractive alternatives to minimize these drawbacks of flexible colonoscopy. Further, these techniques come with an added benefit of identifying pathology outside the colon.

Colonoscopic biopsies provide the first source of tissue for most cases of inflammatory and neoplastic diseases of the colon. With the epidemiological change in the colorectal lesions, investigating and categorizing different gastrointestinal lesions based on their histopathological appearances will aid in evaluating the status of colonic lesions.

Aims and Objectives

To correlate clinical, colonoscopic and histopathological findings in lower gastrointestinal lesions.

Materials and Methods

The study was undertaken in the Department of Pathology of a tertiary health care centre in southern India over the span of two years i.e. September 2014 to August 2016. All colonoscopic biopsies received over the study period for HPE were included in the study. Relevant clinical details along with colonoscopy report were provided with the colon biopsy.

Inclusion Criteria: All new cases reporting to the Gastroenterology Department, who underwent

colonoscopy and biopsy, with all clinical details available were included in the study

Exclusion Criteria: All previously diagnosed cases and those on follow up were excluded from the study. Cases with inadequate clinical/colonoscopic data were excluded from the study.

Statistical Analysis: Statistical Analysis was carried out using IBM SPSS statistics 2016 software, 2x2 contingency tables and Fisher's exact test.

Results

During the study period, ninety-eight colonoscopic biopsy specimens were examined histologically with assessment of clinical and colonoscopic data. The age range was observed to be wide from the youngest aged 7 months to the oldest aged 87 years. Cases were clustered in ages 40-70 years with 22 cases each in ages 41-50 years and 61-70 years. Of the 98 cases, 69 biopsies were from males and 29 from females with a male to female ratio of 2.3:1. Graphical representation is shown as under (Table 1)

Table 1. Age Vs Sex Distribution in all cases

	Up to 30 years	31-40 years	41-50 years	51-60 years	61-70 years	Above 70 years	TOTAL
Male	13	11	14	9	14	8	69
Females	1	0	8	8	8	4	29
TOTAL	14	11	22	17	22	12	98

Patients presented with a wide range of symptoms, with Bleeding per rectum was the most common complaint, seen in 59 cases followed by weight loss seen in 20 cases. Of the 59 cases of bleeding

per rectum, 1 case had associated anaemia while 6 cases had associated weight loss. Following is the summary of clinical presentations of my cases. (Table 2)

Table 2 Clinical presentation in all cases

Clinical Features	No. of cases	Percentage (%)
Anaemia	2	2.04
Anaemia + Weight loss	8	8.16
Bleeding PR	52	53.06
Bleeding PR + Anaemia	1	1.02
Bleeding PR + Weight loss	6	6.12
Chronic Constipation	1	1.02
Chronic Diarrhoea	1	1.02
Diarrhoea + Weight loss	1	1.02
Diarrhoea + Pain Abdomen	1	1.02
Pain Abdomen	16	16.33
Pain Abdomen + Mass PR	1	1.02
Rectal Prolapse	2	2.04
Weight Loss	5	5.10
Lymphadenopathy	1	1.02
Total	98	100.00

Colonoscopy findings of the 98 cases revealed predominantly inflammatory signs (mucosal thickening, erosions and ulcerations) in 22 cases

followed by ulceroinfiltrative growth in 17 cases and closely followed by polypoidal lesions in 16 cases. (Table 3) (Fig 1-2)

Table 3. Colonoscopy findings in all cases

Lesion	No. of cases	Percentage (%)
Mucosal Thickening	4	4.08
Inflammation	3	3.06
Mucosal Thickening + Inflammation	13	13.27
Mucosal Thickening + Inflammation+ Erosions	2	2.04
Mucosal Thickening + Inflammation + Erosions + Ulceration	22	22.45
Strictures	1	1.02
Polyps	16	16.33
Soft Tissue Mass	1	1.02
Ulceroinfiltrative Growth	17	17.35
Ulceroproliferative Growth	15	15.31
Ulceroinfiltrative Growth + Proliferative Component	4	4.08
Total	98	100.00



Fig1. Ulcerative Colitis: Rectum shows nodular mucosa with occasional polyps

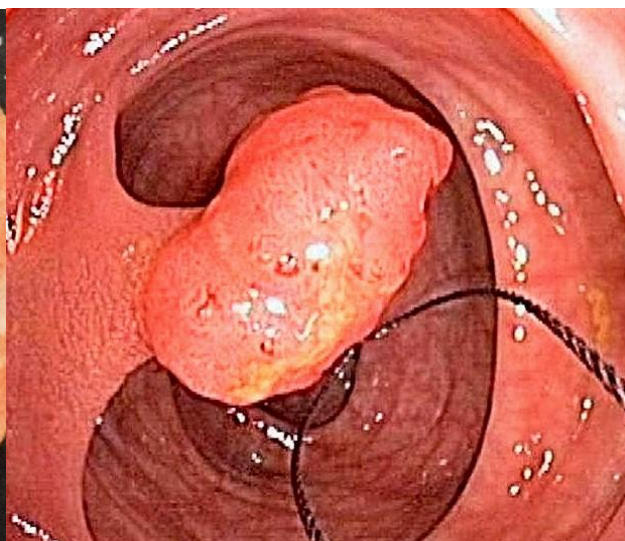


Fig 2. Tubular Adenoma: Sessile polyp in rectum

Biopsies taken from the representative areas in all 98 cases were studied. Forty-Five cases were diagnosed as Non - neoplastic, 43 as Neoplastic, of which 8 cases were Benign and 35 were

malignant. Nine biopsy specimens were inadequate for reporting while 1 biopsy showed normal histomorphology. (Table 4)

Table 4 Histomorphological Classification of all lesions

Categories	No. of cases	Percentage (%)
Non Neoplastic	45	45.92
Neoplastic	Benign	8.16
	Malignant	35.72
nadequate	9	9.18
Normal	1	1.02
Total	98	100.00

Non neoplastic lesions

In this study, 45 cases were non-neoplastic lesions with the predominant group comprising of Proctocolitis (22 cases) closely followed by Ulcerative Colitis (17 cases). Out of the three cases of Granulomatous inflammation, ZN stain

done on the submitted tissue biopsies revealed Acid fast bacilli in 1 case. One case each of Juvenile polyp and Inflammatory polyp was also noted. (Table 5) (Fig 3-4)

Table 5. Distribution of Non Neoplastic Lesions

Non Neoplastic Lesions	No. of cases	Percentage (%)
Non Specific Colitis	18	40.00
Ulcerative Colitis	17	37.78
Proctitis	4	8.89
Granulomatous Inflammation	3	6.67
Inflammatory Polyp	2	4.44
Juvenile Polyp	1	2.22
Total	45	100.00

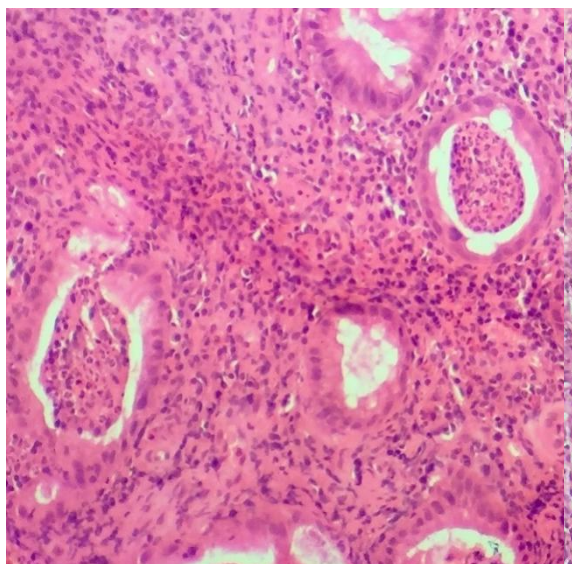


Fig 3. (400X) Ulcerative Colitis-Cryptitis and Crypt abscess

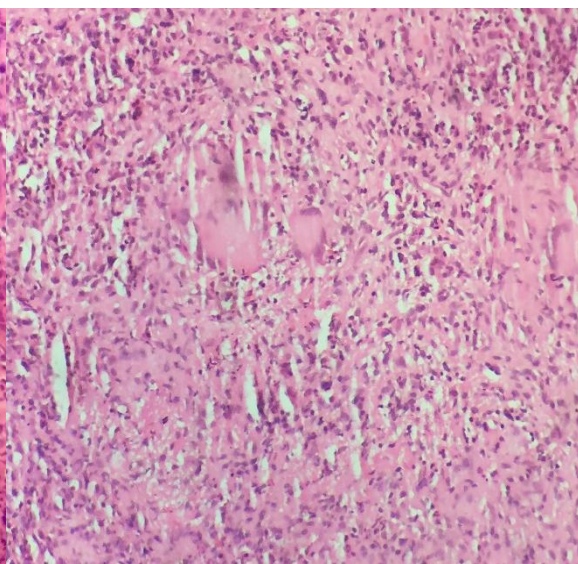


Fig 4. (400X) Granulomatous Inflammation- ill defined epithelioid cell granulomas

Non neoplastic lesions were seen spanning in the entire age range with a peak noted in 41- 50 years (13 cases). However, no significant difference was found between age groups for Non neoplastic lesions of the colon. (Fisher’s Exact T test, p value= 0.304).

Similarly, sex distribution of the Non neoplastic lesions was also studied. Of the 45 Non Neoplastic cases, 36 were among males and 9 were among females. However, no significant difference was found between sex distribution for Non neoplastic lesions of the colon. (Fisher’s Exact T test, p value= 0.484).

The predominant manifestation on the Non neoplastic lesion was bleeding per rectum which was seen in 25 of the 45 cases.

Benign Neoplastic Lesions

In this study, 8 cases of Benign Neoplastic Lesions were diagnosed. Of these, 3 cases were of Tubular Adenoma, 1 was Villous Adenoma and 4 were of Tubulovillous morphology. (Table 6). Age and sex distribution of the Benign Neoplastic Lesions were studied. However, no significant difference between age (Fisher’s Exact T test, p value= 1.000) or sex (Fisher’s Exact T test, p value= 0.357) could be ascertained.

Table 6 Distribution of Benign Neoplastic Lesions

Category	No. of cases	Percentage (%)
Tubular Adenoma	3	37.50
Villous Adenoma	1	12.50
Tubulovillous Adenoma	4	50.00
Total	8	100.00

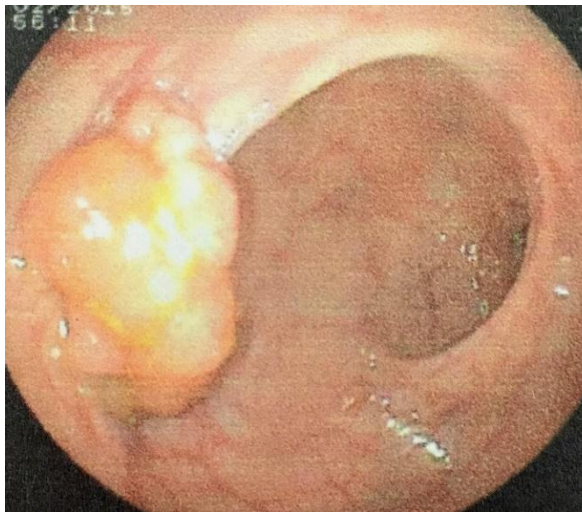


Fig 5. Villous Adenoma: Polypoidal growth in rectum

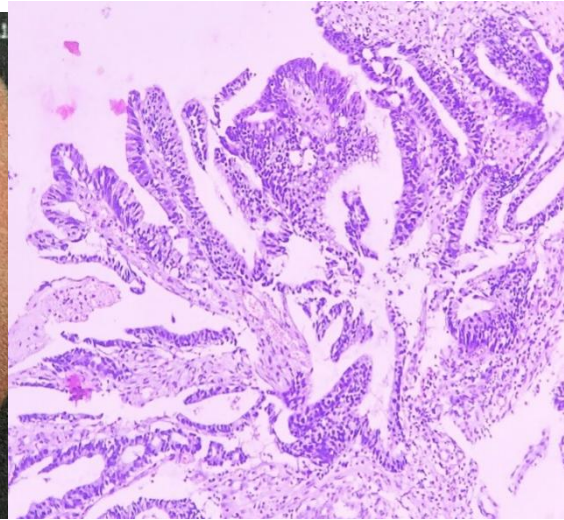


Fig 6. (400X) Villous Adenoma – Villoglandular pattern with low grade dysplasia

Malignant Lesions

Of 98 cases, 35 cases were diagnosed as malignant. The distribution of malignant lesions was as follows- 4 cases (11.43%) of Well Differentiated Adenocarcinoma, 24 cases (68.57%) of Moderately Differentiated Adenocarcinoma and 5 cases of Poorly Differentiated Adenocarcinoma. One case was

diagnosed as Mucin-secreting carcinoma with large extracellular mucin pools comprising 50% of the tumour load. One case of malignant melanoma with interlacing fascicles of spindle to oval cells having vesicular chromatin and prominent nucleoli with intra and extracellular melanin was also observed. (Table 7) (Fig 7-8)



Fig 7. Malignant Melanoma-Polypoidal growth with variegated appearance in the rectum

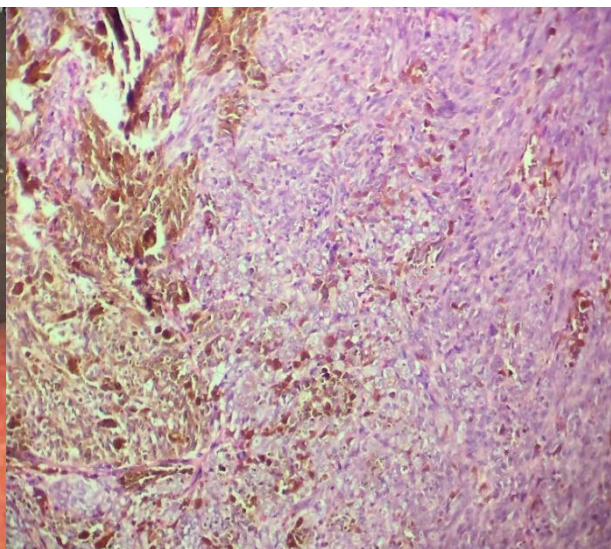


Fig 8. (400X) Malignant Melanoma-Marked intra and extracellular melanin pigment seen

Cases began clustering from 41 - 80 years, with a maximum cases noted 61-70 years. However, no statistical significance was noted between age and malignant lesions (Fisher’s Exact T test, p value=

0.534). Bleeding per rectum was the most common mode of presentation.

Further, 23 cases were among males and 12 among females. Fishers Exact test showed no

significant correlation between sex and malignant lesions. (Fisher's Exact T test, p value= 0.436). Rectum was the most common site of occurrence

of malignant tumours with 22 cases (62.86 %) followed by the 5 cases (14.29%) observed in sigmoid colon.

Table 7. Distribution of Malignant Lesions

Category	No. of cases	Percentage (%)
Well Differentiated Adenocarcinoma	4	11.43
Moderately Differentiated Adenocarcinoma	24	68.57
Poorly Differentiated Adenocarcinoma	5	14.29
Mucin Secreting Adenocarcinoma	1	2.86
Melanoma	1	2.86
Total	35	100.00

Comparison between findings of the colonoscopy and histopathology indicates a minor variation in findings of colonoscopy vs histopathology. Of the 55 cases diagnosed as Benign/ Inflammatory on Colonoscopy, only 49 cases were confirmed as Benign. One case showed features of malignant change and hence was diagnosed as malignant. Five cases could not be diagnosed due to inadequate colonoscopy sampling.

Of the 33 cases diagnosed as malignant on colonoscopy, 31 cases could be confirmed as malignant on histopathology. No definite

diagnosis could be given in 1 case as it contained only granulation tissue while 1 case showed normal colonic mucosa.

Ten cases were found to be suspicious for malignancy and required histopathological examination to come to a definitive diagnosis. Of these 10 cases, 4 cases were diagnosed of benign/ inflammatory nature, 3 were diagnosed as malignant while the 3 remaining biopsies contained inadequate specimen and hence a repeat biopsy was demanded. (Table 8)

Table 8 Comparison between Colonoscopy and Histopathological findings

Investigation	Colonoscopy (No. of cases)	Histopathology (No. of cases)			
		Benign / Inflammatory	Malignant	Inadequate	Normal
Benign / Inflammatory	55	49	1	5	0
Malignant	33	0	31	1	1
Suspicious for malignancy	10	4	3	3	0
Total	98	53	35	9	1

Discussion

Colonoscopy is a crucial tool in diagnosis and management of colon lesions. Recent widespread use of flexible colonoscope has increased our knowledge of the pathogenesis and evolution of disease processes affecting the gastrointestinal tract.⁹

In our present study, in a period of two years 98 colonoscopic biopsies were received in the Department of Pathology. Of these biopsies, 69 biopsies were from males and 29 were from females. Various studies conducted in India and

other western nations have shown similar findings with male predominance.^{10,11}

The most common clinical presentation in this study was per rectal bleeding seen in 60.2 % cases followed by weight loss in 20.4 % cases. These findings were similar to another study conducted by Chaitanya et al in which per rectal bleed was the most common presentation seen in 71 % cases followed by constipation seen in 48.9 % cases.¹²

Our findings with regard to percentages for Non Neoplastic, Benign Neoplastic and Malignant lesions correspond to those observed in the study

series of R. Teague et al¹³, Rajbhandari M et al¹⁴, Sidney J et al¹⁵ and Chaitanya et al¹³ where non neoplastic lesions were maximum in occurrence.

Non Neoplastic Lesions:

In the present study 45 cases were diagnosed as Non Neoplastic. Out of these 18 cases were diagnosed as Non Specific Colitis while 17 cases were diagnosed as Ulcerative Colitis. The findings were similar to other studies done by Rajbhandari M et al¹⁴ and Karve et al¹⁶ where Nonspecific Colitis was the most common finding.

Neoplastic lesions (Benign):

It is believed that colon cancer evolves through a series of morphologically identifiable stages: colon epithelial hyperplasia followed by formation of adenomas that progressively enlarge and ultimately undergo malignant transformation.^{17,18}

In the present study, 08 cases of Benign Neoplastic Lesions of colon were observed. Out of these, 3 cases were diagnosed as Tubular Adenoma, 1 case was diagnosed as Villous Adenoma and the rest 4 cases were diagnosed as Tubulovillous Adenoma.

Though our study found almost equal number of Tubular adenoma (3 cases) and Tubulovillous adenoma (4 cases), other studies have shown tubular adenoma as the most common Benign neoplastic lesion of the colon.^{12,16}

It is important to diagnose these Adenomatous polyps as they pose an increased risk of development of cancer. A study done by Nusko et al reported colorectal polyps as an independent predictor of malignancy. The study stated the risk of developing adenocarcinoma is 1% in adenomas of up to 1cm in size, 10% in adenomas from 1- 2 cm in diameter and 50% in those greater than 2 cm in diameter. Only 4% adenomas less than 6 mm diameter, and 16% of those between 6 - 10 mm are reported to have unfavourable histology.^{19,20}

Malignant Lesions

CRC is a formidable health problem worldwide, being third most common in males and second most common in females.¹³ It is a disease affecting individuals beyond the sixth decade of

life. However, in recent years there has been an increased incidence of colorectal cancers in younger age group.²¹

Studies conducted in the industrialised countries have shown a higher median age of development of colon cancer. Study by Smith et al shows a median age of 68 years (range, 25–88 years) in men and a median of 69 years (range, 33–93 years) in women.

Studies indicate that the age incidence of colorectal cancer in developing countries is lower as compared to developed countries; about 10 years' age difference has been reported in many studies.²²⁻²⁴ In the present study of 35 malignant cases, the mean age of presentation for colon cancer was 60 years. Other studies done in India by Deo et al reported a mean age at presentation of 45.3years²⁵ while study done by Karve et al¹⁶ reported a mean of 49.4 years. Majority of malignant cases were seen in males (23 cases) in accordance to other studies.^{26,17}

Histologic Grade of Tumor

The present study shows Moderately differentiated carcinoma as the most common histological finding. The present study is in accordance with the study series of Laishram RS et al²⁷, Rangaswamy et al²⁸ and Karve et al¹⁶ wherein the most common histological grade was Moderately differentiated adenocarcinoma while the study conducted by Shyamal et al²⁹ showed well differentiated adenocarcinoma as the most common histological grade.

Conclusion

The present study was performed on colonoscopic biopsies of 98 patients received in the Department of Pathology. The aim was to correlate the clinical, colonoscopic and histopathological findings in these patients. The development of Flexible Colonoscope has facilitated early diagnosis of multiple disorders of the colon. A comprehensive histopathological study of these can help in formulating effective therapeutic strategies and prevent associated morbidity and mortality.

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