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The Study of Epidemiology, Clinicopathology and Current Management in Patients of Colorectal Malignancies in Northern India

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: Colorectal malignancy is the third most common malignancy worldwide and the incidence in India is showing an increasing trend. Rapidly increasing incidence rates could result from epidemiological factors including age , race, diet, environmental exposures, and acquisition of modern lifestyle. This study was conducted to describe the epidemiological trends, clinicopathologic characteristics and management of CRC in our settings.
Methods: This prospective study was carried out from November 2020 to November 2022 in the Department of Surgery, at Jawaharlal Nehru Medical College, Aligarh. All histologically confirmed

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cases of colorectal cancer were included. The data was collected and analysed using IBM SPSS Statistics for windows, version 25.

Results: A total of 54 patients with colorectal malignancy were in the study. Males outnumbered females with a Ratio of 1.24.Most of the patients were below 40years of age (42.8%) and the mean age was 45.27±14.208 years. 32 patients (57.1%) were non-vegetarian and 24 patients (42.8%) were vegetarian (P value >0.05). 19.6% of patients had a smoking addiction, 5.3% used tobacco and 3.5% of patients were alcohol drinkers (P value <0.0001). 3 patients(5.3%) had a positive family history of carcinoma or polyposis in their first-degree or second-degree relatives(P value <0.0001). Bleeding per rectum was the commonest presentation (33.9% followed by pain abdomen (26.7%). The highest number of lesion was seen in the rectum alone (46.4%), followed by ascending colon alone (19.6%).On endoscopy, 29(51.7%) patients had circumferential annular growth, 21(37.5%) patients had exophytic mass, 3(5.3%) patients had polyposis masses and 3(5.3%) ulcero-infiltrating mass. Non-mucin-secreting adenocarcinoma was the commonest pathological finding (62.5%), followed by mucin-secreting Adenocarcinoma (30.3%) and signet ring cell carcinoma (7.1%). 32 (57.1%) patients had well-differentiated lesions, 17(30.3%) had moderately differentiated lesions and 7(12.5%) patients had poorly differentiated lesions. The majority (60.7%) of the participants have lymph node involvement. 51 patients (91.1%) underwent surgeries and 5 patients (8.9%) were given neoadjuvant chemo-radiation therapy. There was no mortality during the study period.

Conclusion: Colorectal malignancies are common in our settings and shows a trend towards younger age groups. We recommend screening high-risk groups for early diagnosis and better management.

Keywords: Colorectal; cancer; colon; rectum; chemotherapy; young age.

ABBREVIATIONS

CRC : Colorectal cancer;
DALYs : Disability adjusted life years;
NSAIDs : Non steroidal anti inflammatory drugs;
CEA : Carcinoembryonic antigen;
APC : Adenomatous polyposis coli;
RFA : Radio frequency ablation;
EGFR : Epidermal growth factor receptor;
GLOBOCAN : Global cancer observatory;
HDI : Human development index;
HNPCC : Hereditary non polyposis colon cancer;
FAP : Familial adenomatous polyposis;
VAT : Visceral adipose tissue;
CT : Computed tomography;
FDG-PET : Fluorodeoxyglucose -positron emission tomography ;
WHO : world health organisation;
MRI : Magnetic resonance imaging;
AV : Anal verge;
QoL : Quality of life;
MSI : Micro satellite instability;
BMI : Body mass index;
AJCC : American joint committee on cancer;
SSP : Sessile serrated polyp;
GI : Gastrointestinal;
NICE : NBI International colorectal endoscopic;
NBI : Narrow band imaging;
MS : Microsoft;
SD : standard deviation;
CECT : Contrast enhanced computed tomography;
AYA : Adolescent and young adults;

SES	:	*socioeconomic status;*
OPD	:	*Out patient department;*
RT	:	*Right;*
LT	:	*left;*
LAR	:	*low anterior resection;*
CTRT	:	*chemotherapy plus radiotherapy;*
fb	:	*followed by;*
APR	:	*abdominoperineal resection;*
NM adenocarcinoma	:	*Non mucin secreting adenocarcinoma;*
HTN	:	*hypertension;*
DM	:	*diabetes mellitus;*
FOLFOX	:	*5-Fluorouracil, leucovorin calcium, oxaliplatin;*
FOLFIRI	:	*5-Fluorouracil, leucovorin calcium, irinotecan;*
CAPOX	:	*Capecitabine, oxaliplatin.*

1. INTRODUCTION

Colorectal cancers (CRC) are the 3rd most common malignancies worldwide and second in terms of mortality [1,2]. It accounts for 10% of all cancers and is the second leading cause of disability-adjusted life years (DALYs) for cancer worldwide [3,4]. It ranks second in cancer-related deaths overall and is the leading cause in men younger than 50 years [5].

The incidence in India is showing an increasing trend. As per the cancer registry program the incidence is 8.5% [6]. In recent years, the diagnosis of colorectal malignancy is showing new trends from genetic study to advancement in molecular and imaging techniques. In our scenario, the diagnosis of colorectal malignancy is late, and hence the overall outcome of treatment is usually poor.

Colorectal cancer is often caused by the non-cancerous expansion of mucosal epithelial cells. Polyps are benign growths that can develop slowly for 10-20 years before turning malignant. The most frequent kind is an adenoma or polyp formed by granular cells, which create the mucus that coats the large intestine. Although the risk of cancer increases as the polyp becomes bigger and only approximately 10% of all adenomas proceed to aggressive malignancy. Adenocarcinoma is an invasive malignancy that develops from such polyps and accounts for 96% of all colorectal malignancies [7].

Epidemiological factors of colorectal cancer include age, race and family history of colorectal cancer. The risk of developing colorectal cancer increases with age, Africo American shows a higher risk and a positive family history shows the highest risk. There is no marked difference in incidences in males and females [8]. Multiple factors have been implicated in the development of colorectal cancer. Non-modifiable risk factors like hereditary disorders like Hereditary non-polyposis colonic cancer (HNPCC), Familial adenomatous polyposis (FAP), colonic polyps, Inflammatory bowel disease, abdominal radiation, cystic fibrosis, genetic mutations (p52, K-Ras, Her 2 neu). Individuals who have had cancer, a history of colon polyps, inflammatory bowel disease, diabetes mellitus, or cholecystectomy are at a significantly increased risk for CRC. Lifestyle variables are also essential in the genesis of CRC. The evidence shows that overweight and obesity, physical inactivity, cigarette smoking, alcohol consumption, long-term use of NSAIDs and inappropriate dietary patterns (a diet low in fibre, fruits, vegetables, calcium and dietary products and high in red and processed meat) increase CRC risk. In addition, gut microbiome, age, gender and race and socioeconomic status are known to influence colorectal cancer risk [8,9].

Diagnosis is based on clinical presentation like anaemia due to occult bleeding, fatigue, constipation, altered bowel habits, tenesmus, mucus in stool, etc. The patients usually present with obstruction, due to lack of awareness and unavailability of any program to tackle the issue. Old patients more commonly present with anorexia. Right-sided malignancies are usually ulcerative and present as bleeding and left-sided malignancies are usually obstructive in nature. Rectal cancers present as bleeding per rectum [10]. In addition to clinical signs and symptoms, there are many diagnostic modalities like fecal occult blood test, colonoscopy, biopsy, tumour markers (CEA levels), blood tests, radiological modalities like CT scan , MRI, PET- CT, endoscopic ultrasound, and virtual colonoscopy [11,12].

The key diagnostic hurdles include pre-operative staging and imaging methods that can accurately

detect lymph node illness and/or micro-metastatic disease. This would affect patient care significantly [7,13].

Access to early diagnosis and treatment of CRC for better survival is possible. Highlighting the current status of CRC, it's development, risk factors, and management is crucial in creating public awareness as well as assessment of the burden of disease.

2. METHODOLOGY

The study was an observational, prospective study carried out from November 2020 to November 2022 in The Department of Surgery, Pathology and Radiotherapy at Jawaharlal Nehru Medical College, Aligarh. All the patients having signs and symptoms of colorectal cancer underwent per-operative investigations to make the diagnosis of colorectal carcinoma.

Inclusion Criteria:

- Patients giving well-written informed consent for the study
- Patients with 16 years or more age
- Patients with a diagnosis of colorectal cancer

Exclusion Criteria:

- Patients not giving consent for the study were excluded
- Age 15 years and less were not included in the study
- Patients whose diagnosis came out to be other than colorectal malignancy were not included
- Patients with benign neoplasms of the colon and rectum were excluded

The patient profile details were taken including age, gender, area of residence (urban or rural), socioeconomic status, addictions, dietary history, family history and other risk factors.Socioeconomic status stratification is done on the basis of the Modified Kuppuswamy scale. A History of symptoms which include bleeding per rectum, anaemia, pain per abdomen, abdominal distension, vomiting, inability to pass stool and flatus, the altered bowel habits, along with the duration of symptoms was taken. Family history was also asked. History of other comorbid conditions condition like diabetes mellitus, hypertension and details regarding past history of any significant cardiac or respiratory history, history of any drug intake and personal history was taken including addiction.General examination of the patient including the assessment of vitals i.e.pulse, blood pressure, temperature, respiratory rate, and Glasgow coma scale. Detailed per abdominal examination, digital rectal examination, and proctoscopic examination of the patient was done.All patient underwent routine biochemical investigation which included blood counts, renal function test, PT/INR, total protein, liver function test, triple test, etc. Imaging studies conducted vary from Radiographs, ultrasound, Computed tomography (CT) scan, magnetic resonance imaging (MRI) to Positron emission tomography-computed tomography (PET-CT). Invasive imaging included lower GI endoscopy (Image 1). It not just detected the site and type of growth but also endoscopic of mass lesion biopsies were taken and sent for histological diagnosis. Carcinoembryonic antigen levels were taken into account. It is a poor prognosis marker and correlates with reduced overall survival after surgical resection of colorectal cancer.

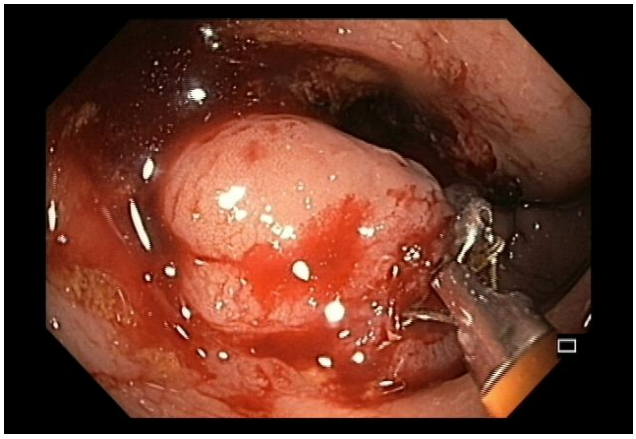

Image 1.

Pathological Study: According to the pathological stage, grade and type, neoadjuvant therapy, surgical or palliative treatment were given to the patient. In surgical resection, the histopathological specimens were sent. Depending upon histopathological report, adjuvant therapy was given.

Pathological staging was done by TNM staging (tumour, nodes and metastasis).

2.1 Management

Management was broadly divided into palliative or curative. Surgical management was decided on the basis of the location of tumor. In ascending colon tumor right hemicolectomy was done. In transverse colon tumor resection and anastomosis was done. In descending colon tumor left hemicolectomy was done. In rectal malignancy low anterior resection or abdominoperineal resection depends on tumour's distance from the anal verge. In patients presenting with acute intestinal obstruction or in patients with metastatic lesions, palliative colostomy or ileostomy were made.

In colonic malignancies, adjuvant chemotherapy was given and no role of neo-adjuvant chemo radiation. In rectal malignancy, neo-adjuvant chemoradiation is done (NACRT) followed by surgery and adjuvant Chemo radiation. Various regimens of chemotherapy were followed including FOLFOX, CAPOX, FOLFIRI.

Based on the histopathology of the tumor samples, tumor was divided into Mucin-secreting or Non-Mucin secreting Adenocarcinoma or signet ring cell carcinoma and pathological TNM staging was done.After the management, patients were followed-up for 6 months to know any recurrence, residual disease or metastasis.

2.2 Statistical Analysis

The details of the study were entered in the form of MS Excel 2016 and analyzed using IBM SPSS Statistical software version 25. Continuous variables were represented in terms of frequency and percentages and Mean and SD. Chi-square statistics were used for inferential statistics. The result was represented in tabular and graphical forms.

Table 1.

Pathological grading		
G1	Well-differentiated	>95% of the tumor is gland forming
G2	Moderately differentiated	50-95% gland formation
G3	Poorly differentiated	<50% gland formation

Table 2.

Pathological types	
Mucinous Adenocarcinoma	>50% of the tumor volume is composed of extracellular mucin
Signet ring cell carcinoma	>50% of tumor cells shows signet ring features characterised by a prominent intracytoplasmic mucin vacuole that pushes the nucleus to the periphery
Non Mucinous Adenocarcinoma	None of the above features

3. RESULTS

In our study, a total of fifty-six patients were assessed as having diagnosis of colorectal carcinoma. Epidemiological factors, risk factors, clinical presentation, pathological type, grade, stage and management were analysed on the basis of data collected from 56 patients with colorectal cancer.

1. Epidemiological characteristics:

Age and Gender: The demographic characteristics of the study population showed a mean age of 45.27±14.208 years. There was more number of participants (42.8%) within the <40years age group which is the AYA population (adolescent and young adult) followed by 40 to 60 years (adult onset) and then greater than 60years (elderly). The gender distribution of the study population showed higher males than females with a M:F Ratio of 1.24.

2. Risk factors

a. Addiction

Table 3.

	No. of patients	Percentage	Chi square	p-value
No addiction	40	71.4	33.880	<0.0001
Smoking	11	19.6		
Tobacco chewing	3	5.3		
Alcohol	2	3.5		
Total	56	100.0		

The Majority of the study population presented with no addiction. 19.6% of the studied population had smoking as an addiction, followed by tobacco chewing in 5.3% of cases and alcohol drinking in 3.5% of the cases studied.

b. Dietary factors

Out of 56 patients of colorectal cancer in our study, 32 patients (57.1%) were non-vegetarian and 24 patients (42.8%) were vegetarian.

c. Family history

In our study, 3 patients (5.3%) with colorectal cancers had positive family history of carcinoma or polyposis in their first degree or second degree relatives.

3. Clinical presentation of the patients

A varied clinical presentation was shown among the participants. Bleeding per rectum was the commonest presentation of the patients in 33.9% cases, followed by pain per abdomen in 26.7% cases, followed by painful defecation in 14.2% cases. Only 5.3% cases presented with features of obstruction.This is graphically represented in Fig. 1.

4. Imaging

All 56 patients of the study population underwent non invasive imaging like CECT or MRI as per requirement and the following locations of the tumour were recorded.

The highest number of lesion was seen in the rectum alone(46.4%), followed by ascending colon alone in 19.6% of the cases. One patient (1.7%) had a lesion in the hepatic flexure and one patient had lesion in the splenic flexure as well.The same have been graphically represented in Fig. 2.

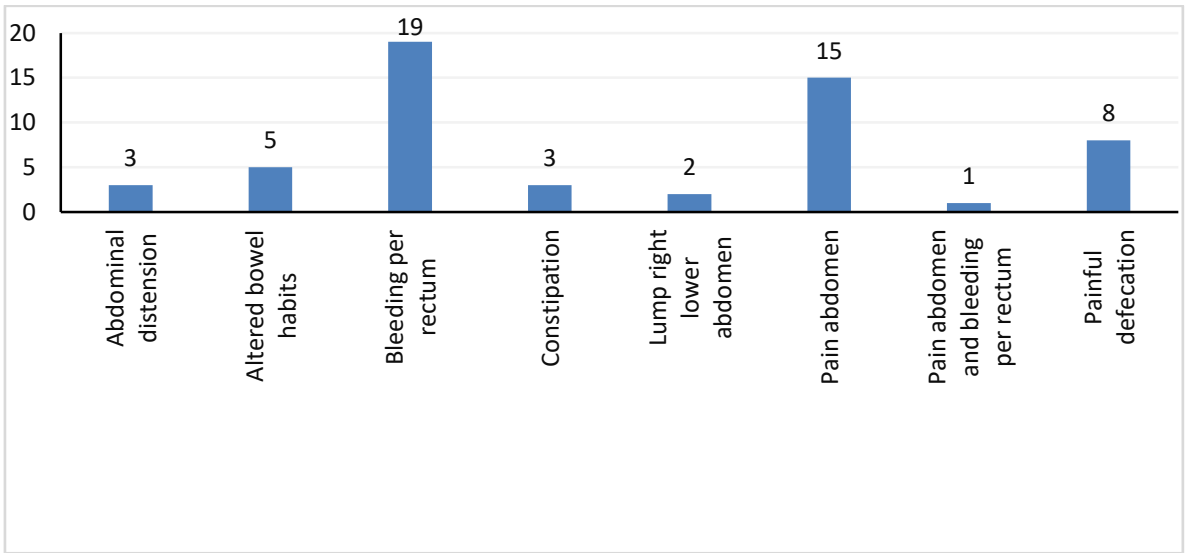

Fig. 1. Graphical presentation of Clinical presentation of the patients

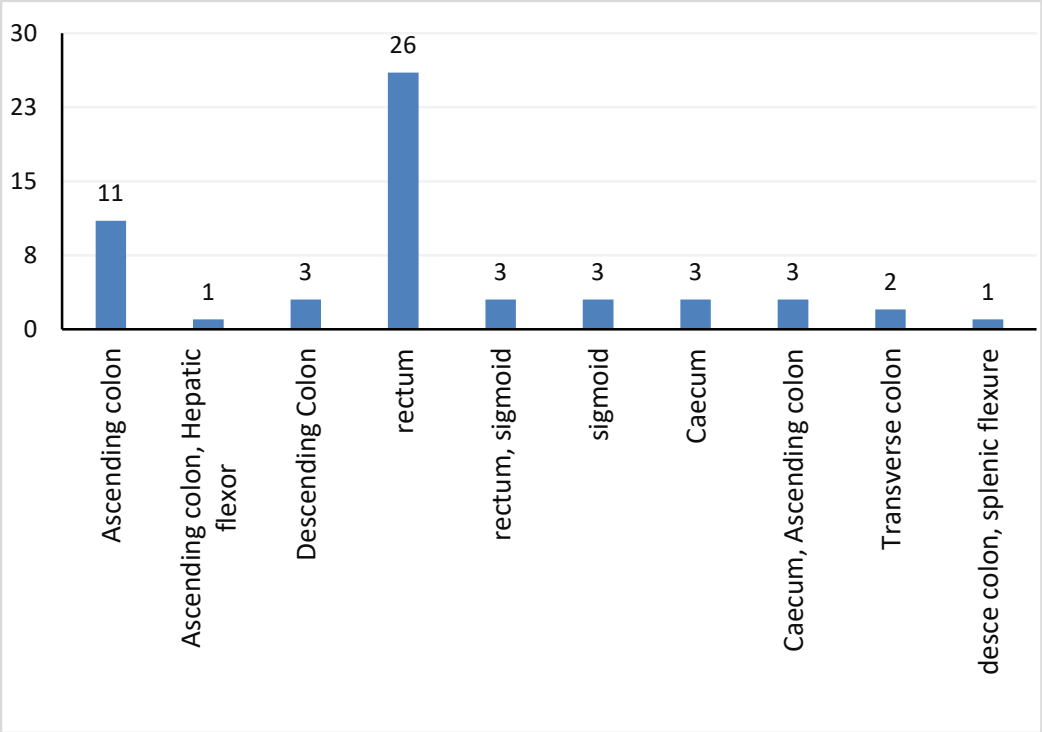

Fig. 2. Graphical presentation of the location of the lesion

5. Endoscopy

Table 4.

	No. of patients	Percentage	Chi square	p value
Exophytic mass	21	37.5	10.15	<0.0001
Polyploid mass	3	5.3		
Ulcerating infiltrative mass	3	5.3		
Circumferencial annular growth	29	51.7		
Total	56	100.0		

Out of 56 patients of colorectal cancer, 29(51.7%) presented as circumferential annular growth on endoscopic imaging, followed by 21(37.5%) patients who presented as Exophytic masses. 3(5.3%) patients presented as polyposis masses and ulcerative infiltrating masses each.

6. Pathological type

Table 5.

	No. of patients	Percentage	Chi square	p value
Mucin secreting Adenocarcinoma	17	30.3	11.56	<0.000
Non mucin secreting adenocarcinoma	35	62.5		1
Signet ring cell carcinoma	4	7.1		
Total	56	100.0		

Non-mucin secreting adenocarcinoma was the commonest pathological lesion in 62.5% of all cases, followed by mucin secreting Adenocarcinoma in 30.3% cases, with only 7.1% cases of signet ring cell carcinoma.

7. Pathological grade:

Table 6.

	No. of patients	Percentage	Chi square	p value
Moderately differentiated	17	30.3	67.89	<0.0001
Poorly differentiated	7	12.5		
Well differentiated	32	57.1		
Total	56	100.0		

Well differentiated lesions were commonest in 32 patients out of 56(57.1%) as compared to moderately differentiated lesions(30.3%) and poorly differentiated lesions in 7(12.5%) patients.

8. Lymph node involvement status:

Majority of the participants had lymph node involvement (60.7% cases).

1. TNM Stage:

The details of the TNM staging have been mentioned. The maximum number of patients had a stage of T3N0Mx in 16.1% cases, followed by T3N1Mx in 6% of the studied cases. The same has been graphically represented in Fig. 3.

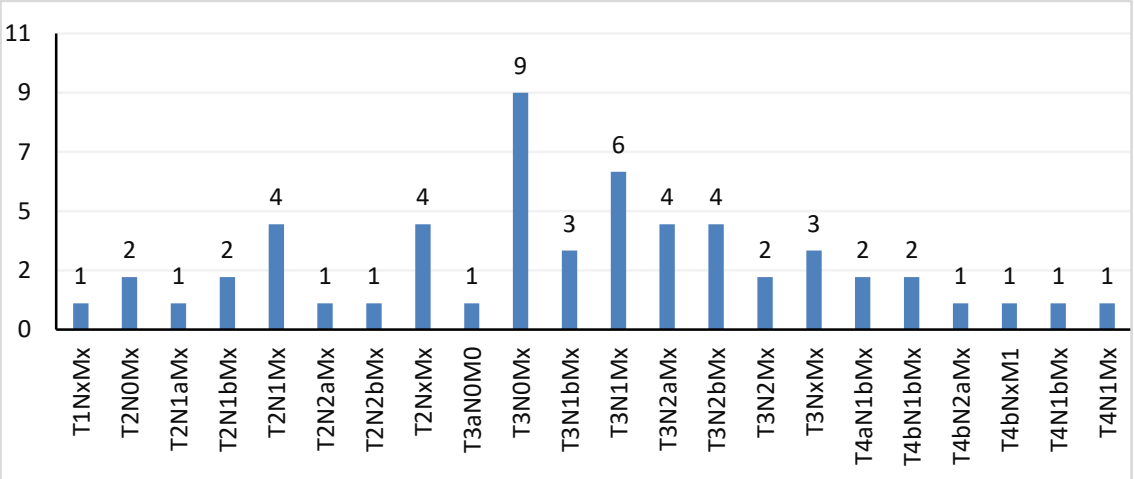

Fig. 3. Graphical presentation of TNM Stage

9. Serum CEA levels (ng/ml):

Table 7.

	Frequency	Percent	Chi sq	P value
<5	6	10.7	87.66	<0.0001
>5	50	89.3		
Total	56	100.0		

S. CEA Levels were classified as above and below 5ng/ml. Majority of the participants(89.3%)had values greater than 5 ng/ml.

10. Management:

A.Neo-adjuvant therapy:

Out of the 56 patients of colorectal cancer in our study, 51 patients (91.1%) were subjected to upfront surgeries and no neo-adjuvant chemo or radiation therapy was given. Rest 5 patients (8.9%) were given neo-adjuvant chemo plus radiation therapy and out of this all were of rectal cancer. This is represented in Table 8.

Table 8.

	Frequency	Percent	Chi square	p value
Received	5	8.9	56.00	<0.0001
Not received	51	91.1		
Total	56	100.0		

Neo-adjuvant therapy was received by only 8.9% of patients and all of them were of rectal carcinoma.

B.Adjuvant Chemotherapy in colon carcinoma:

After surgical resection of colonic cancer, all 24 patients of colon carcinoma were subjected to adjuvant chemotherapy and FOLFOX regimen was initiated in all of them.

Table 9.

	Frequency	Percent	Chi square	p value
FOLFOX	18	75.0	8.34	0.05
FOLFIRI	3	12.5		
CAPOX	3	12.5		
Total	24	100.0		

Out of 24 patients of colon carcinoma, 18 patients(75% of colon cancer cases) responded to post-surgery a FOLFOX chemotherapy regimen. 12.5% of patients of colon cancer who failed to respond to first-line FOLFOX regimen, they responded to the FOLFIRI regimen and 12.5% responded to the CAPOX regimen.

C.Adjuvant therapy in rectal/sigmoid colon carcinoma:

Table 10.

	Frequency	Percent	Chi square	p value
Received	32	100.0	0.0	1.00
Not received	0	0.0		
Total	32	100.0		

All the patients of rectum/sigmoid colon (32 patients) received post-surgical resection adjuvant therapy in the form of chemotherapy [FOLFOX regimen] plus radiation therapy.

In our study, 122 patients who presented with signs and symptoms of colorectal cancer were scrutinised and 56 cases were diagnosed as colorectal cancer. In these 56 patients of study population, the mean age of presentation was 45.27±14.208 years and maximum patients (42.8%) belonged to AYA population group (adolescent and young adult) with a Male:Female ratio of 1.24:1. In risk factors, maximum patients were smokers(19.6%), 32(57.1%) were non-vegetarians and 3(5.3%) patients had positive family history in first and second degree relatives. Clinical presentation was variable with most of them presenting with bleeding per rectum in 19(33.9%) cases out of 56. On non-invasive imaging, the most common site of colorectal cancer was found to be the rectum in 26(46.4%) cases with the most common endoscopic appearance as circumferential annular growth in 29(51.7%) cases. On pathological examination, non-mucin secreting adenocarcinoma was found in a maximum number of patients and well-differentiated was the most common pathological grade. Lymph nodes were positive in 34(60.7%) of the cases and T3N0Mx was the most common pathological stage. Serum CEA value was more than 5ng/ml in 50(89.3%) cases of study population. Surgical resection was done in all patients of colorectal cancer in our study. Out of 56 patients, 51 patients (91.1%) were subjected to upfront surgeries. Rest 5 patients (8.9%) were given neoadjuvant chemo plus radiation therapy and out of this all were of rectal cancer. All the patients of rectum/sigmoid colon (32 patients) received post surgical resection adjuvant therapy in the form of chemotherapy [FOLFOX regimen]

plus radiation therapy. After surgical resection of colonic cancer, all 24 patients of colon carcinoma were subjected to adjuvant chemotherapy and FOLFOX regimen was initiated in all of them. Out of 24, only 18 patients responded to first line FOLFOX regimen and rest five patients were than subjected to FOLFIRI regimen. Out of these 6, only 3 patients responded to FOLFIRI regimen and rest 3 were subjected to second line CAPOX regimen and they responded to it.

4. DISCUSSION

Colorectal carcinoma affects primarily the individuals 50 years of age and older and is much less common in age group less than 40 years. Elzouki et al. showed that the mean age group of patients of colorectal carcinoma was 57.4±12.92 years [14]. In our study, most of the patients (42.8%) were in AYA (adolescent and young adult) population which is less than 40 years. Patients of colorectal cancer present with variety of clinical symptoms. Poornakala et al. showed that bleeding per rectum was the most common complaint in patients of colorectal cancer [15]. In our study, out of 56 patients of colorectal cancer, 19(33.9%) presented with complaint of bleeding per rectum. Colorectal carcinoma can involve any part of the larger intestine varying from caecum and ascending colon to sigmoid colon and rectum. Ayyub et al. showed rectum and sigmoid colon accounted for 68.2% of all cases and ascending and transverse colon were involved in 22.5% cases [16]. In our study, out of 56 patients of colorectal cancer, most of the patients 26(46.4%) had tumor lesions in rectum only, followed by 11(19.6%) patients with lesions in ascending colon and least number of patients (1.7% each) had tumor in hepatic flexure and splenic flexure.Management of colorectal cancer depends on location of tumor and stage of disease. In a study by Gerard Feeney et al., surgical resection of tumor is the gold standard of management for rectal cancer. Neoadjuvant therapy in the form of chemotherapy, radiotherapy or combination of both, has been shown to be effective in reducing tumor burden in advance of curative surgery [17]. In our study, out of 56 cases, only 5 patients(8.9%) received neoadjuvant chemo radiation and all of them were rectal cancer patients. After surgical resection, all the patients of rectal cancer (32 patients out of 56), underwent adjuvant chemo radiation. FOLFOX regimen was given in chemotherapy and radiation therapy was also combined with it to all post operative patients of rectal/sigmoid colon cancer to prevent the recurrence. In our study, out of 24 patients of colon cancer, all of them were subjected to post operative chemotherapy. First line FOLFOX regimen was given and only 18 patients(75%) out of 24 responded to that, followed by FOLFIRI regimen and 3 patients responded to it. Lastly second line CAPOX regimen was given in remaining 3(12.5%) cases and they responded to it.

5. CONCLUSION

Colorectal malignancies are common in our settings and shows trend towards younger age groups. We recommend screening of high-risk groups for early diagnosis and better management.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

CONSENT

Patients giving well-written informed consent for the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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