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Surgery

CLINICAL PROFILE OF CARCINOMA COLON IN KUMAUN REGION OF UTTARAKHAND

KEY WORDS: Colonoscopy, Colorectal Adenocarcinoma, Histopathology

Dr. Prashant Oli General Surgeon, B.D.Pandey District Hospital, Nainital

Prof. Dr. K. S. Shahi Former Hod, Department of Surgery, GMC Haldwani

Dr. Prateek Shakya Assistant Professor, Department of Surgery, GMC Haldwani

Dr. Lalit Choudhary Former Assistant Professor, Department of Surgery, GMC Haldwani

ABSTRACT

Background: The term colorectal cancer refers to a slowly developing cancer that begins as a tumor or tissue growth on the inner lining of the rectum or colon. **Materials and Method:** This observational cross-sectional study assessed the clinical profile of carcinoma colon in kumaun region of Uttarakhand. The total sample size was determined to be a minimum of 30 patients. The study included all biopsy proven cases of carcinoma colon. **Results:** The study population consisted of 69.8% male and 30.2% female patients. Majority of patients of colon carcinoma belong to age group 51-60 years. The clinical features reported were Altered bowel habits (44.2%), Anorexia (41.9%), Generalized weakness (30.2%), Bleed PR (51.2%), Pain abdomen (39.5%), Lump abdomen (23.3%), Anaemia (46.5%) and Obstruction (14.0%). The most common site of tumor was Sigmoid colon (37.2%). Colonoscopy detected Polypoidal growth in 30.2%, Ulcerative growth in 27.9% and Ulceroproliferative growth in 30.2% patients. Histopathology showed that Adenocarcinoma was commonest type (72.1%). Most of the patients repoorted moderately differentiated (55.8%). Stage I was present among 4.7%, II A among 9.3%, III A among 7.0%, III B among 27.9%, III C among 37.2% and IV among 14.0% patients. Most patients presented in late stages as per our study. **Conclusion:** Colorectal adenocarcinoma is a heterogeneous disease that involves multiple tumorigenic pathways. Pathologic analysis provides histologic and molecular information critical to appropriate patient treatment, prognosis assessment, and family counselling.

INTRODUCTION

The term colorectal cancer refers to a slowly developing cancer that begins as a tumor or tissue growth on the inner lining of the rectum or colon.[1] If this abnormal growth, known as a polyp, eventually becomes cancerous, it can form a tumor on the wall of the rectum or colon, and subsequently grow into blood vessels or lymphatics, increasing the chance of metas¬tasis to other anatomical sites.[2] Of the cancers that begin in the colorectal region, the vast majority (over 95%) are classified as adenocarcinomas.[1]

Globally, colorectal cancer (CRC) ranks third in terms of incidence and second in terms of mortality. In 2018, CRC was the most commonly diagnosed GI cancer across the globe with 1.8 million new cases and 881,000 deaths. Among men, it is the third commonest cancer and the fourth most common cause of cancer related mortality, whereas among women, CRC stands second and third in terms of incidence and mortality, respectively.[2]

A relatively low burden of CRC has been reported from low- and middle-income countries (LMIC), and there is a paucity of publications related to CRC from LMIC.[3] The age-standardized incidence rates of CRC reported in LMIC such as India are 7.2 and 5.1 per 100,000 population for men and women in comparison with global CRC incidence rates of 20.6 and 14.3 per 100,000 population, respectively.[4]

The main risk factor for colorectal cancer is age: past the fifth decade of life, the risk of developing CRC is markedly increased, while the onset of colorectal cancer below the age of fifty is rare (apart from inherited cancers).[5] A personal history of colorectal cancer or inflammatory bowel disease (IBD)-the risk in patients with ulcerative colitis is increased by 3.7%[6] while people suffering from Crohn's disease have a 2.5% higher risk of developing colorectal cancer[7] are also important risks for colorectal cancer development. The chronic inflammation found in IBD often produces an abnormal cell growth known as dysplasia.

Another risk factor that can be included in this group is the presence of a positive familial history of CRC in relatives, especially those relatives under fifty years of age at diagnosis. An increased risk due to familial history can be derived from inherited mutations or the environment.[8]

Furthermore, smoking and alcohol consumption have also been shown to increase CRC risk. In the case of alcohol consumption, acetaldehyde (the main metabolite of ethanol) has been described as carcinogenic by increasing the risk of developing colorectal cancer among populations depending on polymorphisms of alcohol metabolism enzymes.[9]

Colonoscopy is the gold standard for the diagnosis of colorectal cancer. It has a high diagnostic accuracy and can assess the location of the tumor. Importantly, the technique can enable simultaneous biopsy sampling and, hence, histological confirmation of the diagnosis and material for molecular profiling. Removal of adenomas using endoscopic polypectomy can reduce cancer incidence and mortality.[10]

The upcoming burden of CRC will bring about a large demand for patient care in areas of CRC detection, staging, and therapeutic interventions, such as surgery, radiation, and chemotherapy. Population-based screening aims at the early detection of colorectal neoplasm's, amenable for curative treatment, and is shown to be an efficient and cost-effective method to lower the disease mortality in developed countries with high CRC incidence.[11] As CRC involves distal large intestine more commonly,[12] proctosigmoidoscopy may be effective screening tool in low resource health centre's.

Only a few studies from India retrospectively reviewed the incidences of colorectal cancer. This study was designed to describe the distribution of the colorectal carcinoma while considering age, gender, site of tumor, tumor pathology in cross sectional pattern.

MATERIALS & METHODS

This observational cross-sectional study assessed the clinical profile of carcinoma colon in kumaun region of uttarakhand after clearance from Board of Studies and Ethical committee in the Department of general Surgery, Dr. Sushila Tiwari Government Hospital, Haldwani, Nainital during the period 2019-2021.

Sample Size

The study population has been calculated by using G-power software with 80% of the power and 5% of the significance level. The total sample size was determined to be a minimum of 30 patients.

Sampling Technique

The study included all biopsy proven cases of carcinoma colon in General Surgery department of Government Medical College, Haldwani and Swami Ram Cancer Hospital, in the study.

Selection of Study Population

The study subjects were chosen as per the inclusion and exclusion criteria. The study included Patients diagnosed with carcinoma colon by histopathological examination and consenting to be the part of study. The study excluded patients not giving consent to be part of study.

Statistical Analysis

The data was entered into the Microsoft excel and the statistical analysis was performed by statistical software SPSS version 21.0. The Quantitative (Numerical variables) were present in the form of mean and SD and the Qualitative (Categorical variables) were present in the form of frequency and percentage.

RESULTS

Forty-three patients with histologic documentation of carcinoma colon were followed by a cross sectional study in Dr. Sushila Tiwari Government Hospital and associated S. R. C. Hospital, Haldwani, Nainital. All subjects were interviewed face-to-face, revealing detailed information about their age, sex, address, occupation, religion, socioeconomic status, education, associated risk factors and clinical presentation and management.

The study population consisted of 69.8% male and 30.2% female patients. Majority of patients of colon carcinoma belong to age group 51-60 years. Most (65.1%) of the subjects were from urban area. Majority of the study population in our study were housewife (30.2%). Majority of the subjects had Graduation (25.6%) followed by Lower secondary education (20.9%) and Upper Primary education (16.3%). The Socioeconomic status according to Kuppuswamy scale showed majority (41.9%) belonged to lower middle class.

Majority (76.7%) of the cases had Non vegetarian dietary habit. The risk factors among study population were Smoking (46.5%), Alcohol (37.2%), Obesity (18.6%), Positive Family h/o (4.7%) and Premalignant condition (4.7%).

The clinical features reported were Altered bowel habits (44.2%), Anorexia (41.9%), Generalized weakness (30.2%), Bleed PR (51.2%), Pain abdomen (39.5%), Lump abdomen (23.3%), Anaemia (46.5%) and Obstruction (14.0%). Overall, most common feature was per rectal bleeding. Bleeding PR and Altered bowel habits were common in left sided growths while proximal growths presented commonly with anaemia or mass per abdomen in our study. 6 patients presented to emergency with features of acute colonic obstruction.

The most common site of tumor was Sigmoid colon (37.2%) followed by Ascending colon (14.0%), Hepatic flexure (11.6%), Rectosigmoid (9.3%), Caecum (9.3%), Descending colon (9.3%), Transverse colon (7.0%) and Splenic flexure (2.3%).

Colonoscopy detected Polypoidal growth in 30.2%, Ulcerative growth in 27.9% and Ulceroproliferative growth in 30.2% patients. Colonoscopy was not done in 5 patients presenting with acute intestinal obstruction. Histopathology showed that Adenocarcinoma was commonest type (72.1%) followed by Mucinous adenocarcinoma in 25.6% and Leiomyosarcoma in 1 (2.3%). Poorly differentiated carcinoma was reported among 27.9%, moderately differentiated among 55.8% and Well-differentiated among 16.3% on histopathological examination. Moderately differentiated carcinoma was commonest grade in our study.

T3 was being most common stage followed by T4. Regional Lymph Nodes positivity (N) was reported among 83.7% patients. Metastatic disease was reported among 14.0% patients. Liver was most common site for metastases. As per AJCC TNM staging, stage I was present among 4.7%, II A among 9.3%, III A among 7.0%, III B among 27.9%, III C among 37.2% and IV among 14.0% patients. Most patients presented in late stages as per our study.

DISCUSSION

Colorectal cancer is a common cancer worldwide with a majority of cases occurring in the developed countries. It should be noted that the population registries in India cover only 7.45% of the population, while worldwide cancer registries cover 21% of the population; so, some amount of under reporting may be possible in India.[4]

The study population consisted of 69.8% males and 30.2% female patients. CRC incidence rates are higher for men in the most regions of the world.[13] Sixty-five percent of the patients in the study by Patil et al.[4] were male. However, there could be a referral bias here in terms of seeking treatment at a referral center. Rajbhandari et al. [14] found that 48% were males and 52% were females with male and female ratio among cancer groups was 1:1.08.

Age

In our study, majority of patients of colon carcinoma belong to age group 51-60 years followed by age group of 41-50 and 61-70 years. However, the prevalence of cases can be seen from 19-74 years. Suliman et al. [15] stated that the mean age of patients at the time of diagnosis was 52.6 years with majority of cases was in the age group above 50 years. Khougali et al.[16] found that the colorectal cancer is the most common in those aged 60–69 years but is almost equally distributed among all age groups aged 30–39 years and above. This study also found that most patients in Sudan present late after the onset of colorectal cancer, which represents a challenge to achieve favorable treatment outcomes. Rajbhandari et al.[14] found that the mean age of subjects was 55.17 years in men and 59.46 years in females with 36% diagnosed with cancer before the age of 50 years.

This finding is in line with that of Gado et al.,[17] who found that in Egypt, about 25% of colorectal cancer patients are aged <40 years. Further, about 45% of the patients in the current study were aged <50 years, while in Saudi Arabia and United States, the percentage of colorectal cancer patients aged <50 years is 37% and 11%, respectively.[18,19] Therefore, these findings suggest that in Arab countries, a larger percentage of colorectal cancer patients are younger compared with that in Western countries. It should be noted that colorectal cancer in those aged <40 years is associated with poor prognosis.

Patil et al.[4] found that the mean age of patients was 47.2 years. Thirty-five percent of the patients were below 40 years of age, and 80% were below 60 years. In a study from eastern India on 168 patients with sporadic CRC, the mean age of presentation was 47.01 years, while it was 58.4 years in a retrospective descriptive analysis of 220 cases of CRC diagnosed at colonoscopy over a five-year period.[19] In another study from central India, on 233 patients over 8 years,

the median age at diagnosis was 43 years with 39% of CRC patients being diagnosed at the age of 40 or younger.[20]

Geographical Distribution

There were 15 (34.9%) patients from rural area and 28 (65.1%) from urban area. This was similar to the studies conducted by Patil et al [4], Rajbhandari et al [14] and Naveen and Kumar [23].

Prevalence According to Education Level, Occupation and Socioeconomic Status

In current study, majority of the subjects had Graduation (25.6%) followed by Lower secondary education (20.9%) and Upper Primary education (16.3%). Majority of the study population in our study were housewife (30.2%).

In present study, the Socioeconomic status according to Kuppuswamy scale showed that 14.0% cases belonged to upper class, 27.9% to upper middle class, 41.9% to lower middle class, 4.7% to upper lower class and 11.6% subjects belonged to lower class.

Dietary Association

In our study, majority (76.7%) of the cases had Non vegetarian dietary habit. Naveen and Kumar [23] stated that 76% patients were non-vegetarian. Increased dietary meat augments the risk of large bowel cancer.

Risk Factors

The risk factors among study population in our study were Smoking (46.5%), Alcohol (37.2%), Obesity (18.6%), Positive Family h/o (4.7%) and Premalignant condition (4.7%).

Mahamud et al [24] found that Positive family history was present in 3.3% cases. More than half of the patients (53.3%) were smokers, 76.7% patients had the history of taking fresh fruits irregularly.

Clinical Features

The clinical features reported were Altered bowel habits (44.2%), Anorexia (41.9%), Generalized weakness (30.2%), Bleed PR (51.2%), Pain abdomen (39.5%), Lump abdomen (23.3%), Anaemia (46.5%) and Obstruction (14.0%). Overall, the commonest feature was per rectal bleeding. Bleeding PR and Altered bowel habits were common in left sided growths while proximal growths presented commonly with anaemia or mass per abdomen in our study. 6 patients presented to emergency with features of acute intestinal obstruction.

Mahamud et al. [24] stated that pain in abdomen was the leading symptom followed by alteration of bowel habit and weight loss. Anaemia was found in 71.6% patients followed by wasting in 70.0% cases. Khougali et al.[16] found that most common presenting symptoms were change in bowel habits (51.5%) followed by rectal bleeding (42.3%), which is the leading cause of anemia in these patients. Studies from Saudi Arabia and Egypt found that about 6% and 9% of colorectal cancer patients had a positive family history, respectively. [22,23]

Suliman et al.[15] noticed that abdominal pain, and rectal bleeding was the commonest symptoms for CRC. This is in agreement with other studies reported in developing countries.[25] Saha et al.[26] reported that bleeding per rectum and features of obstruction are highly suggestive of distal CRC, while abdominal pain and obstruction, anorexia, anemia, and mass are suggestive of proximal CRC.

Site of Cancer

The commonest site of tumor was Sigmoid colon among (37.2%) followed by Ascending colon among (14.0%), Hepatic flexure among (11.6%), Rectosigmoid among (9.3%), Caecum among (9.3%), Descending colon among (9.3%) Transverse colon among (7.0%) and Splenic flexure among (2.3%).

Mahamud et al.[24] reported that Rectum was the principal site of cancer (36.7%) followed by sigmoid colon (33.3%). Cancer in caecum and ascending colon were in 15.0% and 6.7% patients respectively. Khougali et al.[16] reported that the most common site of the carcinomas was rectum (58.9%) followed by sigmoid (8.6%). Our finding differed with the site distribution of colorectal carcinomas reported from developed countries,[27] where distal colon was found to be affected in 53% of the cases and rectum in only 25%.

Suliman et al.[15] stated that Colon cancer was more common than rectum cancer, this finding agreed with the studies done by Gado et al.[17] , Eisa et al.[29], and El-Moselhy et al.[30], who reported similar results as well as the registries from Middle East countries In this study, sparing rectal cancer, colon cancer was more on Right colon (56.2%) which is similar to the cases in developed countries as in the USA and Canada where the most affected site is the proximal colon.[31,32] The relation between gender and proximal or distal colon cancer varies between countries. In the present study, women predominance was observed in distal colon, which matched results of study done by Khiari et al.[33] In Tunisia while in western countries, it is the proximal.

Saha et al.[26] found that the most common location of CRC in this series is distal to splenic flexure. Western reports[34] and few reports from Korea [35] showed that there is a shift of tumor location to proximal part of colon. In our study majority patients had distal colon involvement.

Naveen and Kumar.[21] demonstrated that in various segments of colon involved were rectum (30%), sigmoid (26%), caecum (18%) and ascending colon (6%), transverse colon (4%), splenic flexure (2%) and descending colon (10%). Most common site of involvement for rectum was lower 1/3rd (74%).

Colonoscopic Appearance

Colonoscopy detected Polypoidal growth in 13 (30.2%), Ulcerative growth in 12 (27.9%) and Ulceroproliferative growth in 13 (30.2%) patients. Colonoscopy was not done in 5 patients presenting with acute intestinal obstruction.

Rajbhandari et al.[14] in their study found that (27%) showed chronic nonspecific inflammation, followed by carcinoma (19.8%), non-neoplastic polyps (16.7%), granulomatous inflammation (11.1%), neoplastic polyps (6.3%), ulcerative colitis (3.2%). Miscellaneous lesions: acute focal colitis, eosinophilic colitis was also observed in 15.1% patients.

Histopathology

Histopathology showed that Adenocarcinoma was commonest type in 31 patients (72.1%) followed by Mucinous adenocarcinoma in 11 (25.6%) and Leiomyosarcoma in 1 (2.3%).

The most common histological type of CRC is Adenocarcinoma. This was recorded in the study by Suliman et al.[15] Also histopathological grading in our study showed that 75.6% of the cases with grade II, a finding that is consistent with most studies analyzed.[12] Mahamud et al.[24] found that Adenocarcinoma was the principal histological type (88.0%).

Khougali et al.[16] reported that the most common histological grade of the tumor in this study was Grade 1 adenocarcinoma (50.3%).It should be noted that low-grade cancer is associated with better surgical outcomes and higher quality of life compared with higher grade cancers.

Patil et al.[4] found that 13.0% of patients had signet ring cell carcinomas which are typically associated with poorer prognosis. They were seen more frequently in younger patients (< 40 years) or advanced stages (stage III/IV).

Sixteen percent had mucinous carcinomas, and 25% of the patients had either signet ring or mucinous histology. Most Western studies report a prevalence of 5–15% for mucinous tumors and 1% for signet ring tumors.[36,37]

Histological Grading of Tumor

Poorly differentiated lesions were reported among 12 (27.9%), Moderately differentiated among 24 (55.8%) and Well differentiated among 7 (16.3%) on histopathological examination in our study. Mahamud et al.[24] found that 36.7% were well differentiated carcinoma.

Conventional adenocarcinoma is characterized by glandular formation, which is the basis for histologic tumor grading. In well differentiated adenocarcinoma >95% of the tumor is gland forming. Moderately differentiated adenocarcinoma shows 50-95% gland formation. Poorly differentiated adenocarcinoma is mostly solid with <50% gland formation. In practice, most colorectal adenocarcinomas (~70%) are diagnosed as moderately differentiated. Well and poorly differentiated carcinomas account for 10% and 20%, respectively.[38]

TNM Staging

As per AJCC TNM staging, stage I was present among 2 (4.7%), II A among 4 (9.3%), III A among 3 (7.0%), III B among 12 (27.9%), III C among 16 (37.2%) and IV among 6 (14.0%) patients. Most patients presented in late stages as per our study.

Suliman et al.[15] found that most patients presented with stage II (30.6%) followed by stage III (26.4%) similar to study done by El-Moselhy et al.,[30] most cases presented with stage II followed by stage III. Eisa [29], noticed most patients presented in stage II then stage III as 42.7% and 33.7% of CRC respectively. Suliman et al.[15] found that liver was the most common metastatic site (67.6%).

Mahamud et al.[24] stated that majority of the patients (63.3%) were in advanced stage (stage III and stage IV), similar pattern was observed in our study as majority patients were in stage III. Some forms of surgical treatment were offered to majority of colorectal cancer patients in the study.

In addition to the general limitations of a cross sectional study, this study only included colorectal patients from a single institute and thus has a relatively moderate sample size. As assessing the data of colorectal cancer with wide geographical area is necessary, the authors recommend a national, multicenter study to consolidate the findings of this study and provide precise region-specific data.

SUMMARY & CONCLUSION

While CRC is more prevalent among older patients, the trend of CRC incidence appears to move in an opposite direction to the age. Identifying factors affecting the survival of younger CRC patients along with better treatment strategies and careful follow-up can increase their life expectancy and ease the burden of illness on patients and health system.

Colorectal adenocarcinoma is a heterogeneous disease that involves multiple tumorigenic pathways. Pathologic analysis provides histologic and molecular information critical to appropriate patient treatment, prognosis assessment, and family counseling. As most patients presented at later stages authors recommend implementation of screening of at risk individuals at peripheral health care centers in form of stool occult blood test, colonoscopy or CT colonography according to facilities available at centre to aid in early diagnosis and management resulting in improved outcomes.

Table 1 : Baseline Characteristics of the Study Population

		Frequency	Percentage
Gender	Male	30	69.8%
	Female	13	30.2%
Age (in years)	< 40 years	8	18.6%
	41-50 years	11	25.6%
	51-60 years	12	27.9%
	61-70 years	10	23.3%
	Above 70 years	2	4.7%
	Mean ± SD	51.79±13.78	
Residence	Rural	15	34.9%
	Urban	28	65.1%
Education	Postgraduate	4	9.3%
	Graduate	11	25.6%
	Higher Secondary	6	14.0%
	Lower Secondary	9	20.9%
	Upper Primary	7	16.3%
	Lower Primary	1	2.3%
	Illiterate	5	11.6%
Socioeconomic status according to Kuppuswamy scale	(I) Upper	6	14.0%
	(II) Upper Middle	12	27.9%
	(III) Lower Middle	18	41.9%
	(IV) Upper Lower	2	4.7%
	(V) Lower	5	11.6%

Table 2: Dietary and Risk Pattern Wise Distribution

		Frequency	Percentage
Dietary Habits	Non-vegetarian	33	76.7%
	Vegetarian	10	23.3%
Risk factors	Smoking	20	46.5%
	Alcohol	16	37.2%
	Obesity	8	18.6%
	Premalignant condition	2	4.7%
	Family H/O	2	4.7%

Table 3: Clinical Presentation

Clinical features	Frequency	Percentage
Altered bowel habits	19	44.2%
Anorexia	18	41.9%
Generalized weakness	13	30.2%
Bleed PR	22	51.2%
Pain abdomen	17	39.5%
Lump abdomen	10	23.3%
Anaemia	20	46.5%
Obstruction	6	14.0%
Total	43	100.0%

Table 4: Distribution of Cancer by Site

Site of Tumor	Frequency	Percentage
Ascending colon	6	14.0%
Caecum	4	9.3%
Descending colon	4	9.3%
Hepatic flexure	5	11.6%
Rectosigmoid	4	9.3%
Sigmoid colon	16	37.2%
Splenic flexure	1	2.3%
Transverse colon	3	7.0%
Total	43	100.0%

Table 5: Pattern of Colonoscopic Appearance of Tumour, Histopathological Variation and Histological Grade

		Frequency	Percentage
Colonoscopic appearance	Not done	5	11.6%
	Polypoidal growth	13	30.2%
	Ulcerative growth	12	27.9%
	Ulceroproliferative growth	13	30.2%
Histopathology	Adenocarcinoma	31	72.1%
	Leiomyosarcoma	1	2.3%
	Mucinous adenocarcinoma	11	25.6%
Histological Grade	Poorly differentiated	12	27.9%
	Moderately differentiated	24	55.8%
	Well differentiated	7	16.3%

Table 6:Tumour Stage

		Frequency	Percentage
Primary Tumour (T)	T2	4	9.3%
	T3	22	51.2%
	T4	15	34.9%
	T4a	1	2.3%
	T4b	1	2.3%
Regional Lymph Nodes (N)	N0	7	16.3%
	N1	1	2.3%
	N1a	2	4.7%
	N1b	3	7.0%
	N2	2	4.7%
	N2a	12	27.9%
	N2b	16	37.2%
Distant Metastases (M)	M0	37	86.0%
	M1	6	14.0%
Staging	I	2	4.7%
	II A	4	9.3%
	III A	3	7.0%
	III B	12	27.9%
	III C	16	37.2%
	IV	6	14.0%

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