Colorectal Cancer in Young Adult Population in Kashmir Valley: Tertiary Care Centre Experience

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ABSTRACT

Background: Colorectal cancer (CRC) has been defined and discussed as a disease of middle or late life. However, no age-group is exempt, and adenocarcinoma of the colon has been reported in young age. Malignant disease is frequently found in young adults in our Kashmir valley.

Objective (s): This aim was to study the clinicopathological features, diagnosis, management and outcome of colorectal cancer in young adults under the age of 40.

Material and Methods: This combined Retrospective (January 2002 to May, 2004) Prospective (June 2004 to September 2006) Observational Study was conducted in the Department of General and Minimal Access Surgery, SKIMS. A total of 62 young colorectal carcinoma patients were studied. The case records of all the patients of colorectal cancer less than 40 years of age admitted in the Department of General and Minimal Access Surgery were reviewed retrospectively. In the prospective study, all the patients less than 40 years of age with colorectal carcinoma admitted in our department were registered. Following the confirmation of diagnosis, the patients were subjected to exploratory laparotomy. The nature of the surgical procedure depended upon the intra-operative findings. All the patients were subjected to postoperative chemotherapy and in selected cases to postoperative chemo-radiation. The patients were followed up in General and Minimal Access Surgery and Medical Oncology out patient departments conjointly. The patients were thoroughly examined and investigated on follow up to rule out any recurrence or metastasis.

Results: Most of our patients (83.9%) were admitted through outpatient department (OPD) and only 10 patients (16.1%) were admitted through the Emergency Department. In our study, the male: female ratio was 1.58: 1. The mean age in our study was 30.2 years. Bleeding per rectum was the most common (74.2%) presenting symptom followed by altered bowel habits (72.6%). Carcinoembryonic antigen (CEA) levels show significant decline after surgery/adjuvant therapy. Colonoscopy detected synchronous growths in 5.3% of patients. Rectum was the most common site of lesion (32.2%) while combined rectum and sigmoid colon (including recto sigmoid) accounted for 62.7% of lesions. Resection with intention of cure was performed in 68.3% of patients, palliative procedure in 26.7% and biopsy in 5% of patients. Postoperative complications were recorded and managed accordingly. Typical adenocarcinoma was seen in 80.6% of patients. None of our patients had Dukes stage A presentation. 13.6% of patients had local recurrence and 25.4% had metastasis on follow up.

Conclusion: Colorectal cancers in young adults are quite common in Kashmir valley. Outcome of CRC in young patients is significantly related to the procedure - whether done with curative intention or for palliation. Henceforth, surgical treatment should be radical and optimized with adjuvant therapy where possible to achieve the best prognosis. The diagnosis of colorectal cancer should be done at the early and curable stage for better outcome.

Keywords: Colorectal cancer, Young Adults, Treatment

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INTRODUCTION

Colorectal cancer (CRC) is the most common malignant cancer in the gastrointestinal tract. It represents 13% of all the malignant tumors, and is the second most common cause of death related to cancer affecting men as well as women in the same manner worldwide¹⁻³. Colorectal cancer is the third

most common type of cancer in oncologic pathology⁴. In the

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U.S. colorectal cancer ranks third, only behind prostate cancer and lung cancer in males (8% of all new cancer cases), and behind breast cancer and lung cancer in females (8% of all new cancer cases). Similarly, only lung cancer and prostate cancer are expected to claim more U.S. male lives than colorectal cancer in 2016, and only lung cancer and breast cancer are expected to take more U.S. female lives (8% of total cancer deaths for both genders)⁵. Colorectal malignancies are not as common in India as in most western countries. In India, it is the fourth most common cause of cancer in males and third most common cause of cancer in females⁶. The age standardized rate (ASR) for CRC in India is low at 7.2 per 100,000 population in males and 5.1 per 100,000 populations in women⁷.

Carcinoma of the colon and rectum is predominantly a disease of the elderly population. The pathology is diagnosed more frequently in younger patients, due to changed life style and the progressive aging of the population. However, no age group is exempt, and it had been described to occur in a stillborn by S. Ahlfeld in 1880. The youngest documented patient of colonic malignancy was a 9 month old girl^{8,9,10}. Adenocarcinoma is an unusual disease in patients under 40 years of age, and generally presents as advanced disease. It has been estimated that between 2 and 3% of colorectal cancers occur in patients younger than the age of 40 years¹¹. Men have proportionately higher incidence of rectal cancer than women^{12,13,14}.

Younger patients usually have pre-malignant colonic disease, such as inflammatory bowel disease (IBD) or hereditary polyposis coli. However, *denovo* colorectal malignancy in younger individuals below 40 years of age is being recognized more frequently¹⁵. IBD's are found to be a predisposing factor in 5% of patients¹⁶. Young patients who have had ulcerative colitis (UC) for more than 5 years are particularly predisposed to carcinoma of the colon. Colorectal cancer is a well-documented complication of Crohn's colitis and tends to occur at an earlier age than ordinary colon cancer¹⁷.

Among the genetic and hereditary factors, colonic polyposis syndromes, familial adenomatous polyposis (FAP) and its variants (Turcot, Gardner, and attenuated FAP) and MYH-associated polyposis are the most common. Hereditary nonpolyposis colon cancer (HNPCC) or Lynch

syndrome comprises the non-colonic polyposis category. About 4-6% of patients of familial adenomatous coli will have carcinoma before the age of 25 years and another 6% will be free of cancer until age of 65 years or more. Cancers have been reported at even earlier ages, from 13 to 15 years of age, but such cases seem to be very rare¹⁸. The shift to the western life style with the nutritional transition to increased dietary fat and decreased fiber intake may affect onset of colorectal cancer¹⁶.

The most common symptom of carcinoma of colon in young adults is passage of blood per rectum followed by abdominal pain^{19, 20}. The next most common symptom is change in bowel habits, mainly constipation²⁰. Anemia and weight loss with abdominal pain and altered bowel habits have been encountered in more than half of the patients²¹. Other symptoms include abdominal mass and distention²². Intestinal obstruction (17%) and perforation (9%) may be the presentation. Greater tendency of intestinal obstruction and perforation of left sided tumors is well known. Significantly higher incidence of intestinal obstruction is seen in women than men while no sex difference is seen in perforation, while some reported higher incidence of perforation in women too²³.

Studies have documented that the duration of symptoms is important in determining the outcome of the patients. A delay in presentation of young patients with colorectal cancer has been suggested to be an important factor in prognosis^{24, 25, 26}. Patients identified within 90 days of onset of symptoms have survival rate of 37% while those who had symptoms for more than 90 days, have a survival rate reduced to 25%²⁷.

AIMS AND OBJECTIVES: The aim was to study the clinicopathological features, diagnosis, management and outcome of colorectal cancer in young adults under the age of 40.

MATERIAL AND METHODS

Study Design: Combined Retrospective-Pro prospective Observational Study

Study Area: The study was conducted in the Department of General and Minimal Access Surgery, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar.

Study Population: Patients of colorectal cancer less than 40 years of age admitted in Department of General and

minimal Access surgery.

Study Sample: Our study consisted of 62 young colorectal carcinoma patients; retrospective review of 26 and a prospective study of 36 patients.

Methodology: The case records of all the patients of colorectal cancer less than 40 years of age were reviewed retrospectively. These patients were then followed up in General Surgical and Medical Oncology OPD's conjointly. In the prospective group, all the patients less than 40 years of age with colorectal carcinoma admitted in the Department of General and Minimal Access Surgery were registered. After complete history and thorough physical examination, all the patients were subjected to baseline investigations (complete haemogram, kidney and liver function tests, blood sugar, serum electrolytes), carcinoembryonic antigen (CEA) levels, electrocardiogram, plain X-ray chest and abdomen (in patients presenting with obstruction), ultrasonography of abdomen/pelvis, upper gastrointestinal (UGI) endoscopy (in elective patients), contrast enhanced computerized tomography (CECT) of abdomen (in selected patients). All the elective patients were subjected to primary gastroenterology evaluation to exclude any other underlying primary disease. Though the genetic profile does affect CRC incidence and outcomes of treatment in young colorectal cancers, our patients were not subjected to genetic analysis because of its non-availability at the time of study.

Following the confirmation of diagnosis, the patients were subjected to exploratory laparotomy. Those patients with T3 (Tumor grade 3) lesions were referred to the Department of Radiation Oncology for preoperative chemo radiation for down staging of the lesion before exploratory laparotomy. The surgical procedure performed depended upon the perioperative findings. Resection anastomosis with covering colostomy was done in selected patients followed by closure of the colostomy. In case of unresectable lesions simple palliative measures like colostomy or bypass was done.

The final staging was done according to the operative findings and histopathological examination of the resected specimen as per modified Duke's classification. All the patients were subjected to postoperative chemotherapy and, in selected cases, to postoperative chemo radiation.

During the follow up, the patients were thoroughly examined and investigations (CEA levels, USG abdomen, colonoscopy) done to rule out any recurrence or metastasis.

RESULTS

A retrospective review of 26 patients (41.9%) and a prospective study of 36 patients (58.1%) of young colorectal carcinoma patients (n=62) was performed. Most of our patients (51 patients) were admitted through Outpatient Department (OPD) and only 10 patients (16.1%) were admitted through Emergency Department.

In our study, there were 61.3 % (38) male and 38.7 % (24) female patients with male: female ratio of 1.58: 1. The mean age in our study was 30.2 years and the youngest patient was 17 years old male. The age distribution is shown in table 1. Five of our patients had chronic gastritis, four with duodenal ulcer and one with Chron's disease after gastroenterology evaluation. Two of our patients had family history of colorectal cancer and one had history of gastric carcinoma in first degree relatives.

Bleeding per rectum was the most common (74.2%) presenting symptom followed by altered bowel habits (72.6%). Weight loss was present in 67.7% of patients (>5% of body weight within the last 6 to 12 months or evidence of change in clothing size) and was more common among females (79.2%) than males (60.5%). (Table 2)

In our study mean duration of symptoms was 7.5 months. Minimum duration of symptoms (3 days) was in a male patient who presented with features of obstruction. Maximum duration of symptoms was 18 months. (Table 3)

Table 1: Age Distribution

Age group (yrs)	Male	Female	Total
< or = 20	3	0	3
21-25	10	3	13
26-30	7	10	17
31-35	11	5	16
36-40	7	6	13
Total	38	24	62
P value	0.146		

Table 2: Symptoms of patients

Symptoms	Male	Female	Total
Bleeding per rectum	28	18	46
Altered Bowel Habits			
• Constipation	20	10	30
• Diarrhea	4		4
• Both Alternating	5	6	11
Weight Loss	23	19	42
Pain Abdomen	16	13	29
Anorexia	14	11	25
General body aches and pains/weakness	11	7	18
Tenesmus	7	4	11
Vomiting	5	4	9
Abdominal Distension	5	4	9
Abdominal Mass	3	1	4
Total	38	24	62

Table 3: Duration of Symptoms

Duration of Symptoms (in months)	Male	Female	Total
<or= 3	10	5	15
4-6	11	8	19
7-9	14	3	7
10-12	6	2	8
>12	7	6	13
Total	38	24	62
P-Value	0.868		

CEA levels were available in 21 retrospective and 33 prospective patients. In retrospective group, 57.1% of patients show CEA level greater than 5ng/ml. In contrast, 78.8% of patients in prospective group show CEA level greater than 5ng/ml. Overall, CEA level was normal (<3 mg/ml) in 13% of patients, 3-5ng/ml in 16.7% of patients, 5-10 ng/ml in 33.3% of patients and more than 10 ng/ml in 37% of patients at presentation. CEA levels show a considerable decline after surgery and/or adjuvant therapy which was statistically significant ($p < 0.05$).

Coloscopic/sigmoidoscopic examination was carried out in 38 patients. Synchronous growths were seen in two patients during colonoscopic examination. Most of the lesions ($n=18$) were stenotic and cope could not be passed beyond the growth, 11 lesions were polypoid and 9 lesions were ulcerative growths. No proctoscopy / sigmoidoscopy / colonoscopy was done in 10 patients who presented as acute obstruction. 14 patients had proctoscopically

diagnosed rectal growth.

Most common site was rectum (32.2%) while combined rectum and sigmoid colon (including rectosigmoid) accounted for 62.7% of lesions. Among colonic lesions, left colonic lesions predominate. (Table 4) Right hemicolectomy was most common procedure performed in 13 patients (21.3%). Growth was unresectable in 19 patients (Table 5). One patient refused the surgery and left against medical advice.

Two-thirds of the growths (66.7%) were stenotic, 18.3% were polypoid and 15% ulceroinfiltrative. In three-fourths of patients (45 patients) growth was fixed. Local extension was present in (44)73.3% of patients. Lymph nodes were involved in (43)71.7% of patients. Visceral metastasis in the form of liver metastasis, peritoneal metastasis, parietal wall metastasis, intestines was present in (13)21.7% of patients.

Table 4: Site of Lesion

Site Of Lesion	No. of patients	Percentage
Rectum	20	32.3
Sigmoid Colon	15	24.2
Hepatic Flexure	6	9.7
Splenic Flexure	5	8.0
Recto sigmoid	4	6.4
Caecum Colon	4	6.4
Hepatic Flexure and Ascending	2	3.2
Ascending Colon	1	1.6
Descending Colon	1	1.6
Caecum and Ascending Colon	1	1.6
Caecum ,Ascending Colon and Descending Colon	2	3.2
Rectum and Splenic Flexure	1	1.6
Total	62	100

Table 5: Operative Procedures

Operative Procedure	Number	Percentage
Right Hemicolectomy	13	21.3
Segmental Resection	9	14.7
Abdominoperineal Resection	9	14.7
Left Hemicolectomy	5	8.1
Anterior Resection	2	3.2
Low Anterior Resection	2	3.2
Total Colectomy With Ileo -Rectal Anastomosis	2	3.2
Unresectable		
Sigmoid Colostomy	8	13.1
Transverse Colostomy	7	11.5
Biopsy Only	3	4.9
By-pass(Ileotransverse)	1	1.6
Total	61	100

Fifty three patients had uneventful postoperative hospital stay. Four patients (6.5%) had wound infection. One patient (1.6%) had wound dehiscence in which secondary suturing was done. One patient (1.6%) had anastomotic leak in whom on 4th postoperative day exploratory laparotomy with peritoneal toilet and defunctioning ileostomy was performed. Ileostomy was later closed after 6 months. One patient (1.6%) had retraction of colostomy in which refashioning of colostomy was done. One patient (1.6%) had colostomy prolapse which was managed conservatively by saline packs and ice compresses.

The staging of malignancy was done after histopathological reports. (Table 6 and 7)

Table 6: Histopathology

Histopathology	Male	Female	Total
Adenocarcinoma			
• Well Differentiated	15	11	26
• Moderately Differentiated	8	5	13
• Poorly Differentiated	8	3	11
Mucinous Adenocarcinoma	4	4	8
Signet ring cell carcinoma	3	1	4
Total	38	24	62

Table 7: Modified Duke's Staging

	Male	Female	Total
Stage A	0	0	0
Stage B	6	4	10
Stage C1	7	6	13
Stage C2	15	9	24
Stage D	8	5	13
Total	36	24	60

Of the total of 61 patients on follow-up, 8 patients were found to have local recurrence. 15 patients had metastasis. Liver alone was the commonest site of metastasis found in 7 patients followed by ovary 4 patients, lung 2 patients, brain 1 patient, colostomy site 1 patient. Two patients had combined lung and liver metastasis.

DISCUSSION

From the time of the earliest medical writings to those of the present day, cancer has been defined and discussed as a disease of middle or late life. Likewise, carcinoma of the large intestine is usually thought of as a disease primarily affecting patients in the middle and elderly age group²⁸.

However, no age-group is exempt, and adenocarcinoma of the colon has been reported in a 9 month old infant⁸.

This combined prospective-retrospective study was done to testify this observation. Although exact incidence rate cannot be provided by a hospital-based study, the information would be useful in showing patterns of malignancies in our region.

Patients of the age 40 years or less were selected in our study. Majority of the patients (48.4%) presented in 3rd decade of life. Only 3 patients (4.8%) were less than 20 years of age and correlates well with reports of **Cusack et al (1996)** who reported only 4.8% of patients below 20 years of age²⁹. Youngest patient in our study was a 17 year old male. Mean age in our series was 30.2 years. Mean age in our series is slightly lower than **Walton et al (1976)** series¹⁰. The reason for mean age being lower in our series is because majority of our patients presented in third decade of life. We have observed an increased incidence of colorectal cancers in young adults in our Kashmir. The study done by **Iqbal QM et al.**³⁰ reports that colorectal cancers are quite common in Kashmir valley, that too in younger age group (15-34 year) both among males as well as females. Their study reports 10.5% of colorectal cancer cases among all new cancer patients in the age group of 15-34 year.

There were 38 males (61.3%) and 24 females (38.7%) in our series with male-female ratio of 1.58:1. These findings correlate well with male preponderance shown by some series with male-female ratio ranging between 1.5:1 to 1.7:1^{31,15,32,33}.

All of the patients present with more than two symptoms. Bleeding per rectum was the most common (74.2%) presenting symptom followed by altered bowel habits (72.6%). Weight loss was present in 67.1% and was more common in females. Most of our findings correlate well with the findings of **Johnson and Judd (1959)**, **Adloff et al (1986)**, and **Lee et al (1994)**^{31,19,34}. 16.1% of our patients present with features of obstruction and correlates well with those of **Bulow (1980)**, **Umpleby et al (1984)**, **Domergue et al (1988)** and **Singh et al (2002)**^{21,23,25,35}.

There was a wide range of duration of symptoms with minimum duration of 3 days and maximum duration of 18 months. Mean duration of symptoms was 7.5 months. 45.2% of our patients had duration of symptoms for more than 6 months and it correlates well with that of **Pitluk et al**

(1983)²⁶.16.1% of our patients had short duration of symptoms (in days) and all of them were in obstruction and in those patients short duration of symptoms cannot be correlated with their stage. It did not reflect the actual onset, but a late complication of the disease as pointed out by **Recelde et al (1974)**²⁰.

Colonoscopic / sigmoidoscopic examination was performed in 38 patients. Single lesion was seen in most (94.7%) patients. Synchronous growths were detected in 5.3% of patients on colonoscopic examination. 61.3% of lesions in our study were diagnosed by sigmoidoscopy/ colonoscopy. **Martin et al (1981)** reported 40% of lesions within the reach of sigmoidoscope³⁶.

CEA levels were available in 21 retrospective and 33 prospective patients. In retrospective group, 57.1% of patients show CEA level greater than 5 ng/ml which correlates with **Cusack et al (1996)** series with 51.7% of patients with CEA level greater than 5 ng/ml²⁹. In contrast, 78.8% of patients in prospective group show CEA level greater than 5 ng/ml. CEA levels show a considerable decline after surgery and/or adjuvant therapy which was statistically significant ($p < 0.05$). **Alici et al (2003)** reported that the presence of high serum CEA levels are predictors of poor survival in young patients with colorectal carcinoma(37). **Lin et al (2005)** stated that CEA levels were significant predictor of the overall survival in young patients³⁸.

In our study most common site was rectum (32.3%) followed by sigmoid colon (24.2%) and correlates well with **Smith et al (1989)** reported 32% lesions in rectum and 32% in sigmoid colon³⁹. Together rectum and sigmoid colon (including rectosigmoid junction) accounted for 62.7% of our cases.

In our study, right hemicolectomy was the most common (21.3%) procedure performed followed by segmental resection (14.7%) and abdomino-perineal resection (APR) (14.7%). Curative resection was done in 68.3% of patients and procedure was palliative in 26.7% of patients. In rest (5% cases), only biopsy was taken at laparotomy. These findings correlate well with **Ohman (1982)** who reported 66.7% patients treated with intention of cure and 33.3% for palliation⁴⁰.

Majority of our patients had uneventful postoperative period. Four patients (6.5%) had wound infection. One

patient had wound dehiscence and secondary suturing was done in him. Anastomotic leak, colostomy prolapse and colostomy retraction was noted in one patient each (1.6%).

Abdulla (2003) reported wound infection in 15 patients (5.5%), anastomotic leak in 12 patients (4.4%), hematoma formation in 4 patients (1.1%), urinary bladder disturbance in 2.5%, anastomotic stenosis in 1.1%, anastomotic bleeding in 0.7%, abscess formation in 1.1%, seroma in 0.5%, wound dehiscence in one patient (0.3%)⁴¹. Thus, we see that the complications encountered by us are reported in world literature and are not at a variance with the literature.

No operative mortality (defined as death within 30 days) occurred in our series as reported by other authors also^{11, 15, 25}.

Simona et al (2003) observed significantly higher mortality rate in emergency treated patients than in elective group. It was 11.9% in emergency group and 3.4% in elective group⁴².

Typical adenocarcinoma was present in 80.6% of our patients. The percentage of patients with typical adenocarcinoma in literature ranges between 65-93% and correlates well with our series^{15,20,22,29}. The degree of differentiation was evaluated. Well differentiated adenocarcinoma was most common (41.9%) followed by moderately differentiated adenocarcinoma in 21%. Poorly differentiated adenocarcinoma was seen in 17.7% of patients. Mucinous adenocarcinoma was seen in 12.9% of our patients and correlates well with reported rate of 13% by **Walton et al (1976)** and 11% by **Martin et al (1981)** series^{10,36}.

None of our patients presented with stage A disease. Stage B was seen in 16.7%, stage C in 61.7% and stage D in 21.7%. The disease stages were almost uniformly distributed between the two sexes. In most studies in literature, majority of young patients present in advanced stage (Stage C or D) as in our study. The patients presenting with advanced stage in our study(83.4%) correlates well with the studies in literature as follows:-

Authors	Stage C + D
Howard et al (1975)	79%
Simstein et al (1978)	78%
Safford et al (1981)	80%
Domergue et al (1988)	81%
Present study	83.4

Adjuvant therapy in the form of chemotherapy and/or radiotherapy was given to the patients. 8.3% of patients were given preoperative chemoradiation with a view to downstage the tumour that was later dealt by surgery. These patients used to receive the chemoradiation post operatively as well. 88.3% of our patients were subjected to postoperative chemotherapy. All cases of rectal growths received postoperative radiotherapy (20 cycles). **Rullier et al (2001)** reported that preoperative chemoradiation achieved tumor down staging in 97.7% of patients.⁴³

Patients in our study were on varied follow up, ranging from less than 6 months (for those patients who presented during last few months of study) to 4 years (for retrospective patients). Local recurrence was seen in 13.6% of our patients and correlates with the reported local recurrence of 14% by **Umpleby et al (1984)**²⁵. Metastasis was seen in 25.4% of patients in our series. Liver was the commonest site (11.9%) followed by ovary (6.8%). Lung metastasis was seen in 3.4% of patients, brain metastasis in 1.7% and metastasis at colostomy site in 1.7% of patients. **Cusack et al (1996)** noted liver metastasis in 31%, pelvic in 22%, lung in 14%, bone in 3 %²⁹.

CONCLUSION

Colorectal cancer incidence is increasing among young age, in contrast to the decreasing rates observed for adults in the screened population. Bleeding per rectum is the most common presenting symptom followed by altered bowel habits. Endoscopic examination is important prerequisite in any suspected case of colorectal cancer, further colonoscopy having an added advantage of detecting any other synchronous lesion in the colon as well. Outcome of CRC in young patients is significantly related to the procedure - whether done with curative intention or for palliation. Henceforth, surgical treatment should be radical and optimized with adjuvant therapy where possible to achieve the best prognosis. The diagnosis of colorectal cancer should be done at the early and curable stage for better outcome. Further studies are required to address the early diagnosis and management of colorectal cancer in young adults in our region.

Conflict of Interest- None

Financial Interest - None

Ethical Issue...None

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