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Clinicopathological Profile of Colorectal Cancer in Kashmir

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Abstract

Background: Colorectal Cancer (CRC) is a disease with a major worldwide burden in terms of patient sufferings and cost of treatment. The age-standardized rates of CRC in India are 4.2 and 3.2/lac for males and females respectively.

Objective: To study the Clinico-pathological profile of colorectal cancer patients in Kashmir.

Methods: This 5 year study, conducted in Colorectal Division of Department of General and Minimal Access Surgery, Sher-i-Kashmir Institute of Medical Sciences (SKIMS) in Kashmir, included prospectively all the patients who presented with CRC from August 2014 to June 2016 and retrospectively the data of 3 years of all the patients with CRC was studied. Parameters studied were age, sex, site of lesion, clinical presentations and histology of the lesion.

Results: Among 930 patients included in this study, CRC was most common (24.2%) in the age group of 56 to 65 years. About 19.25% of patients were below the age of 35 years. Male to female ratio was 3:2 (p-value 0.011) and rural to urban ratio was 1.7:1 (p value 0.013). About 96% patients were non-vegetarian. About 50% of the patients had stage III disease at presentation and most patients (75%) presented with change in bowel habits. Recto-sigmoid involvement comprised about 54%. Preoperative CEA levels were elevated (≥ 5.1 ng/ml) in 50% patients. Proliferative type was the most common (n=386; 41.5%) morphology of tumor (p-value <0.0001). Most common morphological type of tumor in youngest age group (15 to 25 years) was infiltrative. Histologically 99% patients had adenocarcinoma and 50% of them were well differentiated.

Conclusion: Colorectal cancer is quite common in Kashmir Valley, involving mostly recto-sigmoid region and majority of our patients present in a locally advanced stage especially in younger age-groups.

Keywords: Cancer; Colorectal; Colon; Rectum

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Introduction

Colorectal cancer is a disease with a major worldwide burden in terms of patient sufferings and cost of treatment. Colorectal cancer is the most common malignancy in the gastrointestinal tract and worldwide colorectal cancer is the 2nd most common cancer among women and the 3rd most common among men [1]. The incidence of rectal cancer is higher in men and that of colonic cancer is higher in women. In high-incidence countries, approximately 25% of colorectal cancers are located in the rectum; 21% among women and 30% among men [2]. The lifetime risk of approximately 6% in Western civilization means that 1 in 17 individuals of the general population will be affected by colorectal cancer making it an important public health issue [3]. Worldwide, CRC shows large geographical differences, with a crude incidence of 6.5/7.7 cases per 100,000 females/males in less developed areas as opposed to 50.9/60.8 in more developed regions. Populations differ in the risk of development of CRC depending upon the race and ethnicity, e.g. Ashkenazi Jews are at a slightly increased risk of CRC [4]. In USA, the incidence of CRC is higher in African-Americans in both sexes as compared with Caucasians which in turn are at higher risk than Asian American, Native Americans, and Hispanic Americans [5]. The age-standardized rates of CRC in India have been estimated to be 4.2 and 3.2/100,000 for males and females, respectively [6]. The crude incidence rate of CRC in Kashmir Valley [7] is 3.65/100,000; it is 3.78 in males, and 3.50/100,000 in females and this is similar to that reported in the rest of India. Colorectal cancer is a multi-factorial disease process. Genetic factors, environmental exposures (including diet), and inflammatory conditions of digestive tract are all involved in the development of colorectal cancer. Colorectal cancers have varied clinical presentation like bleeding per rectum, altered bowel habits, anemia, generalized

Table 1: Correlation between tumor morphology and age.

Age-group (yrs)	No. of Cases (% age)				Total No. of cases (% age)
	Proliferative	Ulcerative	Infiltrative	Ulcero-infiltrative	
15-25	0 (0.00)	0 (0.00)	47 (100.00)	0 (0.00)	47 (5.05)
26-35	86 (65.15)	0 (0.00)	36 (27.27)	10 (7.58)	132 (14.20)
36-45	53 (45.30)	35 (29.91)	29 (24.79)	0 (0.00)	117 (12.59)
46-55	68 (42.5)	47 (29.38)	45 (28.13)	0 (0.00)	160 (17.20)
56-65	100 (44.44)	45 (20.00)	70 (31.12)	10 (4.44)	225 (24.20)
66-75	70 (37.63)	50 (26.88)	66 (35.48)	0 (0.00)	186 (20.00)
Above 75	9 (14.29)	26 (41.27)	28 (44.44)	0 (0.00)	63 (6.76)
Total	386 (41.51)	203 (21.82)	321 (34.52)	20 (2.15)	930 (100)
p-value	<0.0001	<0.0001	<0.0001	-	<0.0001

weakness, obstruction, perforation and peritonitis. Around 15% to 30% of CRCs present as a surgical emergency like obstruction (78%), perforation (10%), or bleeding (4%) [8,9].

Aims and Objectives

The purpose of this study was to study the clinico-pathological profile of colorectal cancer patients in Kashmir at SKIMS, Srinagar; a tertiary care institute.

Materials and Methods

This prospective as well as retrospective study was conducted in Colorectal Division of Department of General and Minimal Invasive Surgery at Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar Kashmir. Prospectively all the patients presenting with colorectal cancer from August 2014 to June 2016 were included in the study. Retrospectively the data of 3 years of all the patients with Colorectal Cancer (CRC) was studied and their records were reviewed from the files in Department of Medical Records, SKIMS. All patients were evaluated with respect to detailed history and physical examination and were investigated to confirm the diagnosis and stage of disease. Study tools were Study-questionnaire, investigations [routine blood tests, CEA, Colonoscopy, USG, CECT and MRI] and histopathological reports. Parameters studied were age, sex, site of lesion, clinical presentations and histopathology of the lesion.

Results

Total of 930 patients were included in this prospective as well as retrospective study, from Jan 2011 to Jun 2016. Male to female ratio in our study was 3:2 (558 *vs.* 372); (p-value 0.011). We had patients from all age groups; from adolescents to elderly. The minimum age of a patient observed was 15 years and the maximum age observed was 87 years. Colorectal cancer was most common in the age group of 56 to 65 years accounting for 24.2% (n=225) of cases followed by 66 to 75 years (n=186; 20%), 46 to 55 years (n=160; 17.2%) and 35 to 45 years (12.6). About 19.25% (n=179) of patients were below the age of 35 years while as only 63 (6.76%) patients presented after 75 years of age. Majority of the patients were from rural areas (n=585; 63%) as compared from urban areas (n=345; 37%) with rural to urban ratio of 1.7:1 (p value 0.013).

History of colorectal cancer in family was present in 242 (26%) of patients; with statistically significant p value of <0.0001. Out of 930 patients, 438 (47.1%) were smokers (p value 0.552). Regarding dietary habit we observed that majority (n=894; 96%) of our patients were non-vegetarian. In most of the patients, symptoms did overlap. However the Most common clinical presentation of the patients in our study was change in bowel habits (n=698; 75%) followed by bleeding PR (n=633; 68%), abdominal pain (n=567; 61%) and generalized weakness (n=316; 44%). However 38 (4%) patients presented with intestinal obstruction and 140(15%) patients had abdominal swelling.

Most common site of involvement was rectum (n=410; 44%) followed by right colon (ascending colon and ceacum) (n=270; 29%), descending colon (n=110; 12%), sigmoid (n=93; 10%) and transverse colon (n=47; 5%). Together rectosigmoid comprise about 54% of total CRC in our study. The most common morphology of rectal carcinoma was ulcerative (n=155; 37.8%) followed by infiltrative (n=138; 33.7%) and proliferative (n=97; 23.7%). While as the most common morphology of right sided carcinoma was proliferative (n=221; 81.8%). Regarding gross tumor morphology, we observed that overall proliferative type was the most common type of tumor in our patients (n=386; 41.5%) with p value of <0.0001, followed by infiltrative (n=321; 34.5%), ulcerative (n=203; 21.8%) and ulcero-infiltrative (n=20; 2.2%). However the most common type of tumor in youngest age group (15 to 25 years) was infiltrative; all the 47 tumors seen in this group were infiltrative (Table 1). Again proliferative type was most common type of tumor in both males and females (41.7% and 41.1% respectively), in both rural and urban patients, in both vegetarians and non-vegetarians and in both smokers and non-smokers.

Histologically most of the patients (n=925; 99.4%) had adenocarcinoma while as non-Hodgkin lymphoma was in 3 patients and small cell carcinoma in 2 patients. Among 925 adenocarcinomas, 49.7% (n=460) were well differentiated, 34.2% (n=316) moderately differentiated and 16.1% (n=149) poorly differentiated. Degree of differentiation varied with the tumor morphology. All the 20 patients with ulceroinfiltrative growth in our study had poorly differentiated histology while as majority of patients (n=219; 58.2%) with proliferative lesions had well differentiated adenocarcinoma. Among 149 patients in our study with poorly differentiated histology, 76 (51%) had infiltrative lesion, 40 (26.8%) had ulcerative lesion and 21 (14.1%) had ulceroinfiltrative lesion while as only 12 (8.1%) had proliferative tumor morphology.

Out of 930 patients, 485 (52%) had pallor and anemia. Pallor was seen in all patients (100%) of ulceroinfiltrative lesions. Also pallor in patients with proliferative lesions was in 65%, with ulcerative lesions in 43.8% and with infiltrative lesions in 38.9% patients. Overall the most common type of tumor leading to pallor was proliferative (51.13%) followed by infiltrative and ulcerative. Overall Bleeding PR

was seen in 68% patients. Most of the patients (n=220; 34.7%) with bleeding PR had infiltrative tumors closely followed by proliferative (32.8%) and ulcerative tumors (29.2%). All patients (100%) with ulceroinfiltrative lesions had bleeding PR and it was present in 91.1% of ulcerative tumors which was statistically significant (p value =0.017).

In our study we found elevated preoperative CEA levels (≥ 5.1 ng/ml) in 418 (44.9%) patients, not elevated (≤ 5.0 ng/ml) in 204 patients (21.9%) and not taken/unknown in 308 (33.1%) patients. Out of 418 cases having elevated CEA levels, 352 (84%) patients had CEA levels in the range of 5 ng/ml to 10 ng/ml.

In our study of 930 patients most (n=463; 49.8%) of the patients presented in stage III followed by stage I (n=230; 24.7%), stage II (n=185; 19.9%) and stage IV (n=52; 5.5%). While as most of the stage III patients presented as stage IIIB (n=283; 61%) and this stage IIIB comprised about 30.4% of the total cases.

Discussion

Colorectal Cancer (CRC) has become one of the commonest malignancies and a major health concern worldwide. It is the third most common cancer in men and the second in women worldwide [1]. According to the reports, every 9 minutes, someone dies from CRC [10]. The incidence is highest in developed countries and low in Asia, Middle East, South America, and Africa [11]. Incidence starts to increase after 35 years of age and rises rapidly after 50 years of age, peaking in seventh decade. More than 90% cancers occur after 50 years of age. However, cases have been reported in young children and adolescents. In our study the most common age group of colorectal cancer was 56 to 65 (24.2%) followed by 66 to 75 (20%) which was consistent with studies of Al-Samawi et al. [12] Majority of our patients were from rural area (63%) as compared with urban area (37%) with rural to urban ratio of 1.58:1. As we have already said that the incidence of colorectal cancer is related to western dietary habits, which is more prevalent in urban population and this paradoxically higher number of patients from rural areas is explained by the fact that our rural population comprise about more than 80% of total population of valley Kashmir. We noticed higher incidence of colorectal cancer in males (60%) as compared to female (40%) which is consistent with the available data [12,13].

Epidemiologic studies have linked increased risk of colorectal cancer with a diet high in red meat and animal fat, low-fiber diet and low overall intake of fruits and vegetables. In our study majority (96%) of the patients were non-vegetarian, taking meat regularly in their diet in the form of chicken, mutton and beef. This is in consistent with studies of Chan et al. [14], Larson et al. [15], Sandhu et al. [16] and Cross et al. [17] Dietary modifications along with secondary prevention measures may have an impact on reducing the mortality from colorectal cancer [18,19]. In our study of 930 patients 438 (47.1%) were smokers which is consistent with findings of various studies in which life style choices such as alcohol and tobacco consumption, obesity and sedentary life style have been associated with increased risk for colorectal cancer [20]. Family history of colorectal cancer was present in 26.02% of patients. In around 10 to 15% of all colorectal cancer cases, a positive family history of Colorectal Cancer (CRC) is observed [21]. It is probable that dietary and other environmental risk factors, acting solely or in concert with genetic factors, influence the aggregation of the disease [22]. The risk associated with a family history of CRC depends on the number of affected relatives and the age at diagnosis [23]. Subjects with one First-Degree Relative (FDR) with CRC diagnosed at age >50 years, have a relative risk (RR) of 2 to 3.15 for developing CRC. Subjects with two (or more) FDRs, with CRC diagnosed at any age, or with one FDR with CRC diagnosed before the age of 50 years, have a relative risk of 4 to 6 for developing colorectal cancer [24]. A Safaee et al. [25] reported a positive family history in 36.4% of the cases. Charles et al. [26] reported that a family history of colorectal cancer is associated with an increased risk of the disease, especially among the young people. Higher frequency of any cancer among family members in the present study is also in agreement with the findings of some other authors.

In our study we found that the most predominant type was adenocarcinoma (n=925; 99.4%). Our results are in agreement with studies of Al-Samawi et al. [12] Kumar Halder et al. [24] and others. Adenocarcinomas compromise the vast majority of colon and rectal cancer (98%). Other rare forms include small cell carcinoma, squamous cell carcinoma, carcinoid, lymphoma and sarcoma. Squamous cell carcinomas may develop in the transition area from the rectum to the anal verge and are considered anal carcinomas. Very rare forms of squamous cell carcinomas of the rectum have been reported [27]. In our study we found Non-Hodgkin lymphoma in 3 cases and small cell carcinoma in 2 cases these results are consistent with other studies [12].

In our study the most common site of involvement was rectum (44%) followed by Ascending Colon (29%) and Descending Colon (12%). This frequency of tumor distribution in colon and rectum is consistent with the studies of Morson and Dawson [28] Halder et al. [24] and other studies [12]. Our results are slightly different as compared to results of Giovannucci et al. [29]. Who had documented approximately 20% 0f colon cancers in caecum, another 20% in rectum, and an additional 20% in rectosigmoid junction. Kumar et al. [30] revealed that rectum was involved in 29.6%, sigmoid colon in 26.5%, ascending Colon in 21%, descending Colon in 17.9% and transverse Colon in 4.9%. In a study by Eisenhardt et al. [31] rectum was involved in 34.6% and colon in 65.4%. Waldron et al. [32] found that 23% of colorectal cancers were right sided (defined as tumors arising from the caecum, ascending colon and hepatic flexure) during their 10 year study period in Birmingham. A 30 year study in Dublin by Crenad et al. [33] revealed that approximately 28% of colorectal cancers were right sided which is comparable to our study.

In our study the most common tumor in young age group (15 to 25 yrs) is infiltrative whereas it is proliferative in older age group (56 to 65 yrs). Overall proliferative is the most common type of tumor in our patients (41%). Our findings are consistent with the study by Falterman KW et al. [34]. The most common type of tumor in both males and females is proliferative followed by infiltrative and ulcerative. Bleeding PR is most common in ulcerative tumors (91%) followed by infiltrative and proliferative tumors. The most common type of tumor leading to pallor is proliferative in 64% followed by ulcerative in 43% and infiltrative in 39%. This corresponds to the study by Posner MC et al. [35].

The mode of presentation of CRC depends upon the site of cancer. Right colon cancers present with weight loss, anemia, fecal occult blood loss, mass in right iliac fossa and the disease more likely to be advanced at presentation. Left colon cancers present with rectal bleeding, change in bowel habits, bowel obstruction, colicky pain and relatively lesser advanced disease at presentation. Overall, the most common presenting symptoms are bleeding PR and change in

bowel habits. It is believed that increased detection of earlier stage colorectal cancer can only be achieved by screening asymptomatic individuals. In our study, the most common mode of presentation was change in bowel habits (75%) followed by bleeding PR (68%) and abdominal pain (61%). Our results were consistent with the study of Smith et al. [36]. However our results were slightly different as compared to results of Lynch et al. [37] in which most common mode of presentation of CRC was bleeding PR followed by change in bowel habits and pain abdomen.

In our study among adenocarcinomas, the well differentiated adenocarcinoma accounted for 49.7%, moderately differentiated adenocarcinoma for 34.2% while poorly differentiated adenocarcinoma for 16.1%. These results are consistent with the study of Al-Samawi et al. [12] and Yoshida et al. [38]. However, our results were different from those of Halder et al. [24] and Eisenhardt et al. [31] in which the most common pathology was moderately differentiated adenocarcinoma followed by well differentiated adenocarcinoma and poorly differentiated adenocarcinoma.

In our study most of the patients presented in stage III (49.8%) followed by stage I (24.7%), stage II (19.9%) and stage IV stage (5.5%). While as most of the stage III patients presented as stage IIIB (n=283; 61%) and this stage IIIB comprised about 30.4% of the total cases. These results were slightly different from studies of Kumar et al. [30]. In which 5.3% of patients presented in stage I, 14.9% in stage II, 40.4% in stage III and 36.8% in stage IV in case of colon cancers while in case of rectal cancers 6.3% presented in stage I, 22.9% in stage II, 47.9% in stage III and 22.9% in stage IV. Eisenhardt et al. [31] reported 40% of patients presented in stage IV, 24.6% in stage III and 32.4% in stage II. Amin et al. [39] found 36% of patients presented in stage IV, 23% in stage III, 30% in stage II, and 11% in stage I. In a study by Chalya et al. [40] 3.3% of cases presented in stage I, 41.6% in stage II, 30.4% in stage III and 24.7% in stage IV.

In our study we found elevated preoperative CEA levels (≥ 5.1 ng/ml) in 418 patients (44.9%), not elevated (≤ 5.0 ng/ml) in 204 patients (21.9%) and not taken/unknown in 308 (33.1%) patients. Out of 418 cases having elevated CEA levels 352 patients had CEA levels in the range of 5 ng/ml to 10 ng/ml (84%). These results were in agreement with other studies [31]. Serum Carcino Embryonic Antigen (CEA) is not recommended as a screening test, but it might be ordered preoperatively to monitor for any recurrence of disease postoperatively. However the data is insufficient to support the use of CEA to determine whether to treat the patient with adjuvant therapy or not [41].

Conclusion

Colorectal cancer is quite common in our Kashmir Valley with majority presenting in advanced stage. Most (96%) of the patients with CRC are non-vegetarians. Incidence of CRC is increasing in younger age group and younger patients present at advanced stage. Lack of awareness about CRC in general population and lack of screening programs are responsible for advanced stage of CRC at presentation. Public awareness through mass-media, screening of high-risk populations, early diagnosis, cost-effective multi-modality treatment and regular follow-up is the call of the time for limiting the morbidity and mortality associated with colorectal cancer.

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