

CLINICAL STUDY OF YOUNG COLORECTAL CANCER IN YANGON GENERAL HOSPITAL

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A hospital based descriptive study was performed during the period of January 2018 to December 2018. 62 young colorectal cancer patients attending to Medical Oncology Department, YGH, who met the inclusion and exclusion criteria, were involved in this study. This study included histologically proved 36 rectal cancer and 26 colon cancer patients. Details of patient's particulars, presenting symptoms, stage, performance status, treatment modalities and response to treatment were recorded. The most common clinical presentation was abdominal pain in colon cancer and bleeding per rectum and tenesmus in rectal cancer. 59.68% of patients had undergone curative resection and 40.32% were done palliative surgery. 9, 38 and 15 patients were given neoadjuvant, adjuvant and palliative chemotherapy, respectively. 27 rectal cancer patients were also treated with radiotherapy. Among 9 patients who were treated with neoadjuvant chemotherapy, only one patient had been performed curative ARR after neoadjuvant therapy. In 38 patients treated with adjuvant chemotherapy, 10 patients had locoregional recurrence and 4 patients showed distant recurrence during adjuvant chemotherapy. 24 patients had no recurrence until the end of adjuvant chemotherapy. In 16 stage IV patients, 1 patient with right ovarian metastasis was treated with debulking surgery followed by adjuvant chemotherapy. This patient showed no recurrence until the end of study. 15 patients were done palliative surgery followed by palliative chemotherapy. 2 patients had partial response and 13 patients were progressive. Most patients are symptomatic at the time of presentation, with the majority having rectal bleeding and chronic abdominal pain. The majority of tumors were located in the rectum, sigmoid colon and ascending colon. The earlier the stage, the more curative surgery and favorable outcome occur. Therefore, it was very important to notify the early symptoms of colorectal cancer.

Keywords: colorectal cancer; young age; Myanmar

INTRODUCTION

Colorectal cancer (CRC) is the second most common cause of cancer mortality after lung cancer in the United States and ranks third in frequency among primary sites of cancer in both men and women (after lung, breast and prostate cancer). Nearly one million cases are diagnosed annually worldwide, accounting for 9% to 10% of human cancers. The lifetime estimated risk for developing CRC in United States is about 5%, with 3% of CRC occurring in patients younger than 40 years of age.¹ As a disease predominantly affecting older individuals, 90% of all CRC have been diagnosed in patients more than 50 years of age. However, an increasing evidence of CRC in patients less than 40 years of age has been reported. When confronting young onset CRC with older patients, issues such as biological aggressiveness, stage at diagnosis and clinical outcomes seem to differ in many aspects.² According to the Yangon Cancer Registry (2016), the numbers of CRC patients enrolled at Medical Oncology Unit, Yangon General

Hospital (YGH) are 393 in total 3584 cancer patients (10.96%). There are 98 patients under the age of 40 years in total 393 of CRC patients (24.93%) and 295 patients over the age of 40 years (75.06%). Data from the American Cancer Society also noticed an increase in the global incidence from 1992 to 2005 among adults between 20 and 49 years, demonstrating a 3.5% increase per year among men and 2.9% per year in women.³ The limited studies reveal a wide range of reported clinico-pathological characteristics and prognosis for young CRC patients. Some studies have demonstrated that young CRC patients presented poor pathological features and advanced stage compared with older patients. Nonetheless, others have found no difference when tumor stage and pathological features were compared with older population.⁴ The purpose of this study is to describe the epidemiological, clinical and pathological characteristics and clinical course of CRC in young Myanmar patients.

MATERIALS AND METHODS

This study was hospital-based descriptive study from January 2018 to December 2018 in Medical Oncology Department, YGH. Study population was newly diagnosed young colorectal cancer patients who registered at Medical Oncology Department, YGH within study period. Inclusion criteria were patients with histologically proven adenocarcinoma of colorectal cancer under 40 years of age and exclusion criteria included patients with concomitant or prior malignancy patients with other histological types rather than adenocarcinoma and patients ≥ 40 years of age. Patient chart and data, imaging facilities (USG, CXR, CT scan), colonoscopy, CEA level, baseline investigations (liver function, renal function, complete blood count and cardiac function including ECHO) were recorded. Types of treatment obtained (Surgery, Radiotherapy, Chemotherapy or best supportive care) were noted. Responses were assessed after 6th cycle and end of chemotherapy. Data collection was done by proforma and data entry, data clean up, data summarization and data analysis was carried out by computer using statistical package for

social science (SPSS) software version 22. Descriptive and summary statistics were carried out.

RESULTS

Among 408 CRC patients registered at Medical Oncology Department, Yangon General Hospital, 78 patients (19.12%) were diagnosed before 40 years of age. According to inclusion and exclusion criteria, 62 patients (26 colon cancer and 36 rectal cancer patients) were included in this study. The mean age of young colon cancer was 29.69 years and the mean age of young rectal cancer was 29.53 years. The youngest age was 18 years for colon cancer and 14 years for rectal cancer. According to age group, both colon and rectal cancers were commonly occurred in the age group of 30-39 years. The male: female ratio was 1.2: 1. Among 62 patients, 9 patients had family history of cancer. The most frequent presenting symptom was abdominal pain (29%). Other symptoms were tenesmus (19.4%), constipation (16.1%), bleeding per rectum (16.1%), change in bowel habit (8.1%), abdominal mass (8.1%) and abdominal distension (3.2%).

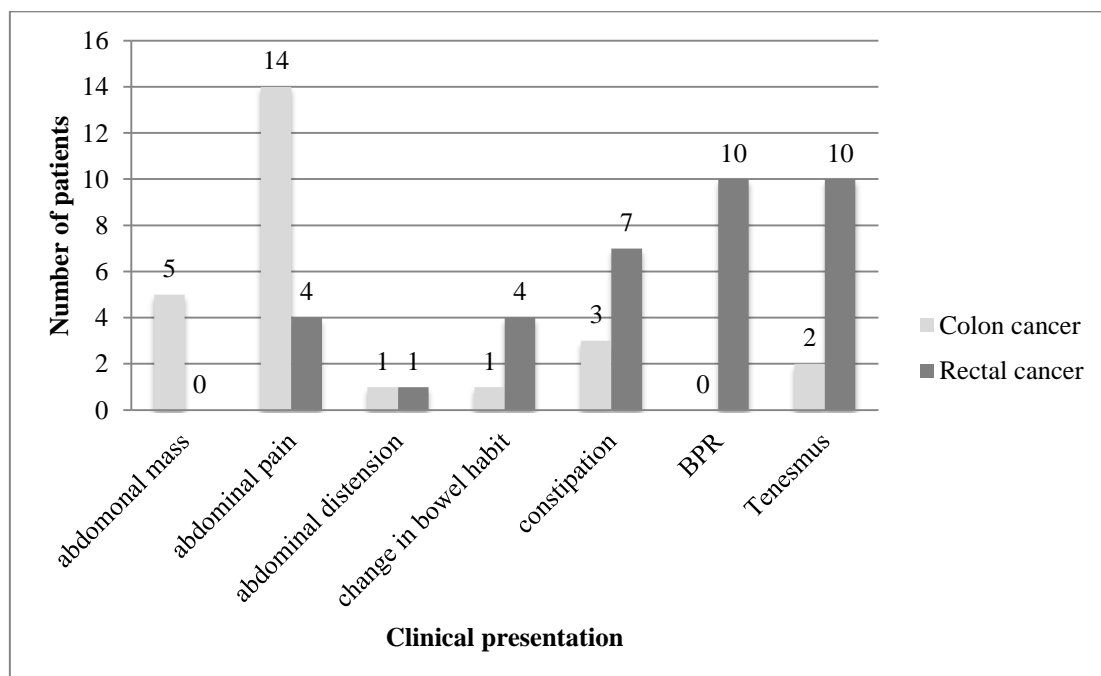


Figure (1) Clinical presentation of young colorectal cancer

(54.8%) of patients showed normal CEA level and (45.2%) had elevated CEA level. The most common location of tumor was rectum (45.2%). Second most common location was

sigmoid colon and ascending colon (14.5%) each. Recto-sigmoid junction tumor was found in (12.9%) and tumor at descending colon was occurred in (3.2%).

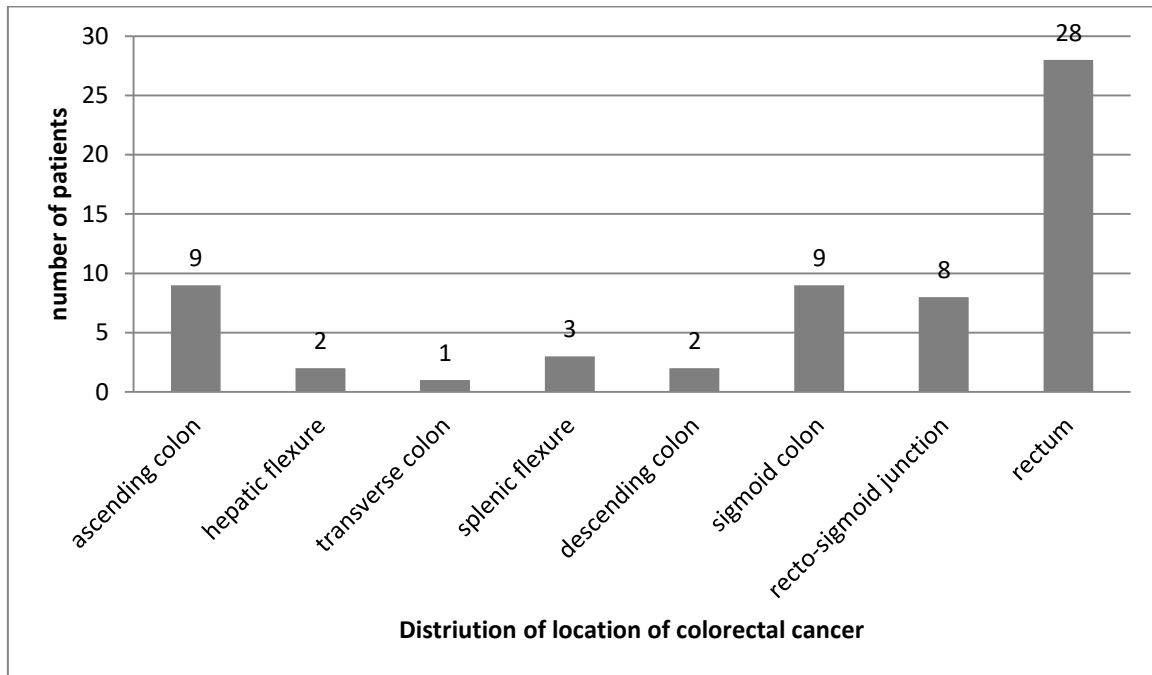


Figure (2) Distribution of location of young colorectal cancer

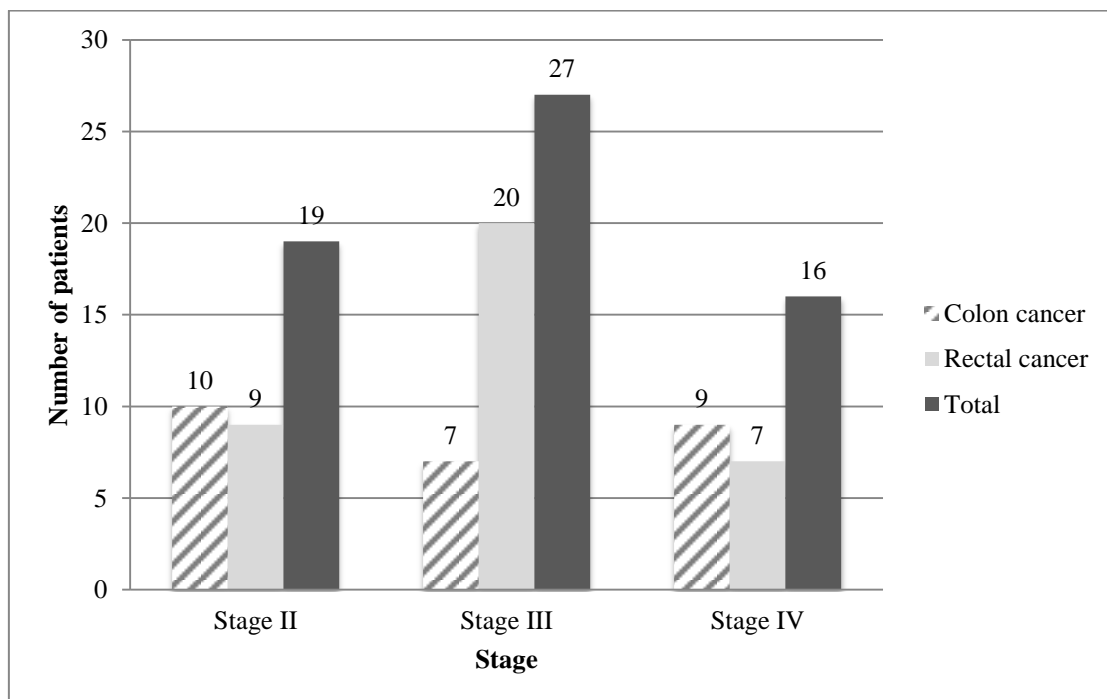


Figure (3) Distribution of stage of young colorectal cancer

The most presenting stage was stage III (43.5%), followed by stage II (30.6%) and stage IV (25.8%). There was no stage I in this study. Adenocarcinoma (unspecified) (58.1%) was the most common histopathological subtype, followed by adenocarcinoma (mucinous) (30.6%) and signet ring cell carcinoma (11.3%). (51.6%) had moderately differentiated histology, (43.55%) had poorly differentiated histology and (4.8%) showed well differentiated histology.

Various surgical procedures were noted; hemicolectomy in 19 patients, palliative colostomy in 19 patients, ARR in 10 patients, laparoscopic ARR in 1 patient, APR in 4 patients and laparoscopic APR in 3 patients, Hartmann's operation in 5 patients and debulking surgery (ARR with appendectomy with right salpingo-oophorectomy for carcinoma of rectosigmoid junction with right ovarian metastasis) in 1 patient. Among 36 young rectal cancer patients in this study, 27 patients (75%) were treated with radiotherapy with curative intent and 9 patients (25%) had no radiotherapy since 6 patients had already stage IV at the time of presentation, 1 had complication such as intestinal obstruction and 2 patients progressed to stage IV before radiotherapy. Among 62 patients, 9 patients received neoadjuvant chemotherapy, 38 patients were treated with adjuvant chemotherapy and 15 patients were given palliative chemotherapy. Various chemotherapy regimens were given; modified de Gramont regimen in 6 patients, FOLFOX regimen in 54 patients and CAPEOX regimen in 2 patients.

Among 38 patients who received adjuvant chemotherapy, 2 out of 17 stage II patients and 8 out of 20 stage III patients were found to have local recurrence and 4 out of 20 stage III patients had distant recurrence during adjuvant chemotherapy. Remaining 24 patients had no recurrence. These 24 patients were reassessed 6 months after completion of adjuvant chemotherapy and the result showed 16 patients had no recurrence, 6 patients had locoregional recurrence and 2 patients had distant recurrence. Among 9 patients who received neoadjuvant chemotherapy, 3

patients had partial response, 2 had stable disease and 4 had progressive disease. Among them, only 1 patient was performed ARR after neoadjuvant therapy. 4 patients were not done surgery due to progressive disease. 2 patients were planning for operation and 2 patients were receiving neoadjuvant radiotherapy at the end of study. Among 15 stage IV patients, who received palliative chemotherapy, 2 patients had partial response and remaining 13 patients had progressive disease during palliative chemotherapy.

DISCUSSION

Colorectal cancer (CRC) is the most common malignancy in the gastrointestinal tract and the third leading cause of cancer associated death in the world. Sporadic colorectal cancer is traditionally diagnosed after the sixth decades of life, and current recommendations for surveillance include only patients older than 50 years of age. However, increasing incidence of young-onset colorectal cancer was noted in many regions across the globe.⁵ Moreover, Vuik FER et al., (2019) study also stated CRC incidence rises among young adults in Europe.⁶

This study was a hospital based descriptive study of young colorectal cancer younger than 40 years of age who were registered in Medical Oncology Department of YGH during the period of January 2018 to December 2018. During this study period, total 408 new cases of colorectal cancer were registered in Medical Oncology Department, YGH. Among them, 78 cases were younger than 40 years (19.12% of all colorectal cancer cases) (YGH cancer registry, 2018).

According to inclusion and exclusion criteria, 62 cases were enrolled in this study group. There were 26 young colon cancer patients (41.9%) and 36 young rectal cancer patients (58.1%). This study included demographic data, clinical presentation, histopathological characteristics, anatomical distribution, presenting stage, treatment modalities given and outcomes in terms of response to treatment, 6 month disease free survival and death.

In this study, the mean age of young colon cancer was 29.69 years and the mean age of young rectal cancer was 29.53 years. According to age group, both colon and rectal cancers were commonly occurred in the age group of 30-39 years. The male: female ratio was 1.2: 1 and therefore male preponderance was observed. In Haleshappa et al., (2017) study, the median age of the study cohort was 33 years (12–40). Majority of the patients belonged to the age group of 30–39 years and there was a male preponderance and it was nearly similar with this study.⁷

In Bouassida et al., (2012) study, the most frequent presenting complaints were abdominal pain (52%), per-anal bleeding (22.5%), change in bowel habit (17.5%) and constipation (17.5%).⁸ In this study, the most frequent presenting symptom was abdominal pain which was occurred in 18 out of 62 patients (29%). Other symptoms were tenesmus in 12 patients (19.4%), constipation in 10 patients (16.1%), bleeding per rectum in 10 patients (16.1%) and change in bowel habit in 5 patients (8.1%).

In Jieun Lee et al., (2016) study, the tumor location of young colorectal cancer was the following in decreasing order; rectum (37%) of patients, sigmoid colon (24%), ascending colon (21%), transverse colon (10%), recto-sigmoid junction (3%) and descending colon (2%).⁹ In this study, the most common location of tumor was rectum which was found in 28 patients (45.2%). Second most common location was sigmoid colon and ascending colon (14.5%) each. Recto-sigmoid junction tumor was found in 8 patients (12.9%) and tumor at descending colon was occurred in 2 patients (3.2%).

Saluja et al., (2014) stated that the most common presenting stage was stage III (45%) followed by stage IV (30%), stage II (20%) and stage I (5%).¹⁰ Among 62 patients in this study, the most presenting stage was stage III which was found in 27 patients (43.5%), followed by stage II which was found in 19 patients (30.6%) and stage IV which was noted in 16 patients (25.8%). There was no stage I young colorectal cancer patient in this study. This will be due to relative lack of knowledge and awareness to

CRC symptoms compared with patients in the developed countries.

In the study, adenocarcinoma (unspecified) (58.1%) was the most common histopathological subtype, followed by adenocarcinoma (mucinous) (30.6%) and signet ring cell carcinoma (11.3%). In study of different clinical characteristics in sporadic young-age onset colorectal cancer in Korea, adenocarcinoma (unspecified) was also the most common histopathological type found in (76.2%), followed by adenocarcinoma (mucinous) (19%) and signet ring cell carcinoma (4.8%).⁹

In this study, 32 patients (51.6%) had moderately differentiated histology, 27 patients (43.55%) had poorly differentiated histology and only 3 patients (4.8%) showed well differentiated histology. Rui Wang et al., (1988-2011) stated that moderately differentiated histology was found in 63.9% of patients, poorly differentiated in 25.9% and well differentiated histology in 8.1%.¹¹

Surgery is the only universally accepted potentially curative treatment for colorectal cancer. Fifty to sixty percent of patients who undergo successful surgery for colon carcinoma have residual micro-metastatic disease. Systemic chemo-therapy is given in an effort to clear micrometastatic disease.¹²

Various surgical procedures were noted; hemicolectomy in 19 patients, palliative colostomy in 19 patients, ARR in 10 patients, laparoscopic ARR in 1 patient, APR in 4 patients and laparoscopic APR in 3 patients, Hartmann's operation in 5 patients and debulking surgery (ARR with appendectomy with right salpingo-oophorectomy for carcinoma of rectosigmoid junction with right ovarian metastasis) in 1 patient.

Jason et al., (2019) found that in contrast to colon cancer, local treatment failures of rectal cancer after potentially curative resections represent a major clinical problem.¹³ Combined modality therapy with RT (chemoRT) is the standard therapy for patients with stage II and III rectal cancer (T3, T4 and nodal involvement).

Among 36 young rectal cancer patients in this study, 27 patients (75%) were treated with radiotherapy with curative intent and 9 patients (25%) had no radiotherapy since 6 patients had already stage IV at the time of presentation, 1 had complication such as intestinal obstruction and 2 patients progressed to stage IV before radiotherapy.

Among 62 patients, 9 patients received neoadjuvant chemotherapy, 38 patients were treated with adjuvant chemotherapy and 15 patients were given palliative chemotherapy. Various chemotherapy regimens were given; modified de Gramont regimen in 6 patients, FOLFOX regimen in 54 patients and CAPEOX regimen in 2 patients.

The response assessment was performed using revised Response Evaluation Criteria in Solid Tumors (RECIST) guideline version (1.1). In total 62 patients, 38 patients were treated with adjuvant chemotherapy. Among those 38 patients, 10 patients (26.3%) had locoregional recurrence and 4 patients (10.5%) showed distant recurrence during adjuvant chemotherapy. Only 24 patients (63.2%) were noted to have no recurrence until the end of adjuvant chemotherapy.

Since the study period was too short, the advantage of adjuvant chemotherapy was not clearly identified by means of survival in this study. Therefore, these 24 patients were reassessed at 6 months after completion of chemotherapy and it was found that 6 patients had locoregional recurrence and 2 patients showed distant recurrence. 12 stage II patients and 3 stage III patients showed no recurrence. Moreover, one stage IV patient who received debulking surgery followed by adjuvant chemotherapy had no recurrence up to 6 months after completion of adjuvant chemotherapy.

Among 9 patients who received neoadjuvant chemotherapy, only 1 rectal cancer patient, who had partial response after neoadjuvant therapy, was performed ARR at the end of my study. 4 patients were not done surgery due to progressive disease. 2 patients were planning for operation and 2 patients were receiving neoadjuvant radiotherapy at the end of study. Saluja et al., also described that among 18 patients of young CRC patients

who received neoadjuvant chemotherapy only 4 patients underwent resection. There was a partial response in 2 patients and stable disease in the other two.

Among 16 stage IV patients, 1 patient had debulking surgery (ARR, appendectomy and right salpingo-oophrectomy) for tumor at recto-sigmoid junction with right ovarian metastasis (T3N1bM1a) followed by adjuvant chemotherapy (FOLFOX – 12 cycles) and adjuvant radiotherapy (50 Gy /25 fractions). This patient had no recurrence until the end of this study. The remaining 15 patients were performed palliative resection followed by palliative chemotherapy. 2 out of these 15 patients (13.3%) had partial response and the remaining 13 patients (86.7%) had progressive disease following palliative chemotherapy.

Progressive disease were highly observed in this study. It may be due to aggressive nature of young onset CRC. Saluja et al., (2014) described that young onset colorectal cancer had aggressive nature when compared to elderly population thereby resulting in advanced disease, which is less resectable at the time of presentation.¹⁰ Moreover, Anele et al., (2019) reported that despite higher rates of adjuvant and neoadjuvant treatment, young CRC were found to have worse disease-free survival compared to older group.¹⁴

During this study, death events were occurred in 13 patients (20.97% of total patients). They were 4 stage III patients and 9 stage IV patients. All patients were died of cancer with disease progression.

CONCLUSION

In conclusion, this study provided the demographic distribution, different clinical characteristics and presentations, treatment modalities and different clinical outcomes of young colorectal cancer. Based on these findings, we can conclude that most patients are symptomatic at the time of presentation, with the majority having rectal bleeding and chronic abdominal pain. The majority of tumors were located in the rectum, sigmoid colon and ascending colon.

The earlier the stage, the more curative surgery and favorable outcome occur. Therefore, it was very important to notify the early symptoms of colorectal cancer. This study will promote increased awareness and aggressive pursuit of symptoms in young patients.

Incidence and prevalence of young colorectal cancer is rising all over the world and becoming a major concern. This study was single center study consisting of small number of patients so that there were many limitations for definite conclusion. Hopefully, we will have more studies on young colorectal cancer patients covering many Oncology Centers in Myanmar in the future.

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