Clinical, morphological and laboratory investigation findings differences between the right and left sided colorectal cancer in a group of Bangladeshi patients

R Paul[1], M Kamal[2], F Begum[3], T Saha[4], T Talukdar[5]

Abstract

Background: Colorectal cancers (CRCa) are a global oncologic problem challenging physicians, surgeons and pathologists. A cross-sectional descriptive study was conducted among 35 cases of CRCa to see the clinical, morphological and investigation findings differences between right and left sided CRCa and loss of heterozygosity status in colonic cancer cells of these cases. Cancers arising from the left versus the right side of the colon have been shown to differ with respect to epidemiology, gross and morphology. Right sided colonic cancer (Rt.CC) patients were in younger age group, overweight and had smoking history. They had larger size, mostly exophytic type tumour that extended more up to pericolic fat. They commonly presented with abdominal pain. On the other hand left sided colonic cancer (Lt.CC) patients were in older age group, less overweight and smoking history, smaller sized, mostly ulcerating type tumour. Among the 30 cases of adenocarcinoma, 27 were left sided and only 3 were right sided. On the other hand only 5 (14.3%) were mucinous adenocarcinoma of which 2 were right sided and 3 were left sided. Poorly differentiated adenocarcinoma (1=20% vs 2=6.6%) and mucinous adenocarcinoma (2=40% vs 3=10%) were found more on right side compared to the left. Lt.CC had more lymphocytes infiltrating tumour. Rt.CC were mostly associated with ³50% extracellular mucin production. Lymphovascular invasion was found more in the Lt.CC compared to the right. Rt.CC were in more advance stage and high grade compared to the left side. Nodal metastasis in Rt.CC was more compared to that of left side.

Key words: Colon cancer, Colorectal cancer etc. ***J Cox Med coll 2018;5(2): 4-11***

Introduction

CRCa is one of the common malignancies throughout the world. It is the third most diagnosed cancer in the United States. Each year in the United States there are more than 130,000 new cases and 55,000 deaths (15% of all cancer related deaths) from CRCa[1].

CRCa is also prevalent in other developed countries. The incidence is lower in less developed regions of the world compared to the west. It is as much as 30-fold lower in India, South America, and Africa[1]. However, the picture is changing, as life style is altering. In Korea it is now the fourth most common cancer in both genders[2]. In Japan where the incidence was previously very low, rates have now risen to intermediate levels (similar to those in the United Kingdom)[1]. CRCa is relatively uncommon in the Indian sub-continent. In India the incidence of CRCa was found to be 4.2 and 3.2 per hundred thousand male and female populations respectively[3]. Peak incidence of CRCa is between ages 60 and 70. Fewer than 20% of cases occur before age 50. Males are affected slightly more than females[1]. There is some evidence of further increase in its occurrence particularly in young black[4]. The incidence of CRCa in Bangladesh is not known, it appears to be common and occur in slightly younger age group with slight male preponderance. Average age at diagnosis is 10 years less than the developed countries[5,6]. CRCa in some Bangladeshi patients may present in younger age and at a more advanced stage[3]. Rt.CC are more common in the elderly, in blacks and in patient with diverticular disease[4]. Tumor location seems to be an important prognostic marker for colon cancer[7].

There is growing number of data suggesting that carcinomas of the right and left colon should be considered as different tumor entities. Right and left-sided colon cancers are significantly different regarding epidemiological, clinical, and histological parameters. Patients with Rt.CC cancers have worse prognosis. These differences may be due to underlying genetic cause that account for distinct carcinogenesis and biological behavior. The impact of these findings on screening and therapy remains to be defined[8].

Rt.CC is more common in patients older than 60 years of age and in women. Patients with Lt.CC are diagnosed at a more early stage of disease and have a more clinical expression of symptoms[7]. On the

1. Dr. Rupash Paul
Assistant professor, (Pathology)
Cox`s Bazar Medical College.
2. Prof Mohammed Kamal
Professor of Pathology
Bangabandhu Sheikh Mujib Medical University (BSMMU)
3. Dr. Ferdousy Begum
Associate Professor, (Pathology)
Bangabandhu Sheikh Mujib Medical University (BSMMU)
4. Dr. Trina Saha
Medical officer
Eidgaon Union Health Subcenter, Sadar, Cox's Bazar
5. Dr. Tutul Talukdar
Resident Surgeon
250 Bed District Sadar Hospital, Cox's Bazar

Correspondence:
Dr. Rupash Paul
e-mail : rupash_pal@yahoo.com

other hand Lt.CC is dominant in men and patients of middle age. Poorly differentiated, mucinous and signet ring cell tumors were frequently seen in Rt.CC[9]. In addition rectal cancers have more advanced staging and fewer curative resections[10].

Tumors in the proximal colon (right) tends to grow as polypoid / exophytic masses that extends along one wall of the capacious caecum and ascending colon. Whereas carcinoma in the distal colon (left) tends to be annular, entophytic encircling lesions that produce napkin-ring constriction of the bowel[1]. The patients with Rt.CC tended to have larger tumors, less differentiated tumors such as poorly differentiated adenocarcinoma, signet ring cell carcinoma and mucinous carcinoma and higher prevalence of distant lymph node involvement and peritoneal metastasis than those with Lt.CC[11]. Mucinous adenocarcinoma was significantly more frequent in right sided colon than in left sided colon[12]. The distribution of CRCa in Bangladeshi population observed in Raja's study is 74% in left colon (mostly in rectum) and 26% in the right colon. Lt.CCs were less well differentiated than the right[6]. In another study Lt.CC (63%) was found more than that of Rt.CC (37%) in Bangladeshi people[5].

Caecal and Rt.CC present as fatigue, weakness and iron deficiency anemia. These bulky lesions bleed easily and may be discovered at an early stage. Lt.CC present as occult bleeding, changes in bowel habit or crumpy left lower quadrant discomfort. The chance for early discovery and successful removal should be greater for patients with lesions on the left side because these patients usually have prominent disturbances in bowel functions such as melena, diarrhea and constipation. Carcinoma of the rectum and sigmoid colon tend to be more infiltrative at the time of diagnosis than proximal lesions and therefore have a somewhat poorer prognosis[1].

In Iceland there was a study over 2293 cases of CRCa. Higher TNM-stage, larger tumors, vessel invasion, mucinous type, high grade and expanding tumor border occurred more frequently in right versus left-sided lesions while annular and polypoid tumors were more common in Lt.CC[13].

CRCa is a multifactorial disease process. Etiology contributing from environmental factors includes dietary factors, obesity, alcohol intake, smoking and life style changes. The molecular event that leads to CRCa is heterogeneous and includes genetic and epigenetic abnormalities. Analysis of molecular alteration in left and right sided CRCa reveals distinct pathways of carcinogenesis[8,14].

Objectives

1. To see morphological and histologic features of right and left sided CRCa.
2. To see clinical presentations of right and left sided CRCa.
3. To see the investigation findings in right and left sided CRCa.

Materials and method

A cross sectional study was carried out in 35 specimen of CRCa patients in department of Pathology, BSMMU, Dhaka during the period of May 2110 to January 2011. Cases were collected from BSMMU and private hospitals and clinics of Dhaka city.

Inclusion criteria

a. Histologically confirmed cases of adenocarcinoma of the colon.

b. Cases with complete clinical information and investigation report who underwent surgical resection.

Exclusion criteria

a. Clinically suspected CRCa subsequently proved to be non-malignant lesions after histological examination.

b. Non Hodgkin lymphoma and other non epithelial tumors of the colon.

c. Patients who had cancers both in the right and left colon, either synchronously or metachronously.

Observations and Results

Socio-demographic characteristics of the respondents

Age distribution of the CRCa cases

The age range was from 14 years to 76 years with a mean age of 42.9 ± 13.7 years. Out of 35 cases maximum number (12, 34.8%) of patients belonged to the age group 40-49 years, followed by 8(22.9%) cases in 30-39 year age group 7(20.3%) cases in 50 59 year group.

Location of the tumour

Among the 35 respondents, maximum (30, 85.7%) had tumour on the left side and only 5 (14.3%) on the right. Age distribution of right and Lt.CC cases were compared. Persons having Lt.CC were higher age range than persons having Rt.CC.

Sex distribution of the respondents

In this study, out of total 35 cases, 21 (60%) cases were male and 14 (40%) cases were female with male to female ratio of 1.5:1. In the Rt.CC, male patients were 2 and female patients were 3. On the other hand, among the patients having Lt.CC, 19 were male and 11 were female patients.

Occupation of the respondents

All the female patients were housewife and were 14 (40%) in number. Among the male patients, 9 (25.7%) were in service followed by 6 (17.1%) in business, 3 (8.6%) in agriculture, 2 (5.7%) were rickshaw puller and 1 (2.9%) was student.

Predisposing factors

BMI (Body mass index) of the respondents

Most of the patients (71.5%) suffering from CRCa were within the normal range (18.5-24.99) of BMI.

Only 4 (11.4%) respondents had <18.5 BMI. Persons having Lt.CC with increased BMI (25) were less in proportion to that persons having Rt.CC (1:1.25)

Positive family history:

Maximum number (28) of patients did not have any family history of gastrointestinal cancer and only 7 (20%) had history of different types of malignancy in their family members. Respondents having both sided tumours proportionately had same positive family history (1:1).

Smoking habits of the respondents

Maximum numbers of patient (23= 65.7%) were non-smoker in relation to 12 (34.3%) smokers. All the respondents were non-alcoholic. Among the non-smokers, 4 had Rt.CC and 19 had Lt.CC. Among the smokers, 11(36.6%) had Lt.CC and only one had (20%) Rt.CC. Lt.CC patients were more smokers in proportion to that of right (1.8:1).

History of meat intake

Patients with Rt.CC, maximum number (4 within 5) took an average 4 times meat in a month. But patients having Lt.CC, took more meat than right. Among them, most took (11) 3-4 times in a month followed by 8-12 times and 0-1 times (6 in each), 1-2 times and 2-3 times (3 in each) and only one took 16 to 20 times in a month.

Clinical features

Table I: Clinical feature of right and Lt.CC.

Clinical features	Right sided tumour (Total 5 cases)	Left sided tumour (Total 30 cases)	Total (35 cases)
Per-rectal bleeding	2(40%)	30(100%)	32(91.42%)
Pain in anal region	0	8(26.6%)	8(22.85%)
Abdominal pain	5(100%)	6(20%)	11(31.42%)
Lump in abdomen	1(20%)	0	1(2.85%)
Anorexia	2(40%)	5(16.6%)	7(20%)
Sense of incomplete defecation	0	4(13.3%)	4(11.4%)
Irregular bowel habit	0	2(6.6%)	2(5.71%)
Constipation	0	3(10%)	3(8.57%)
Weight loss,	2(40%)	7(23.3%)	9(25.7%)
Weakness	0	1(3.3%)	1(2.85%)

Size of the tumour

The maximum diameter of the tumours ranges from ?15cm to ?61cm. Rt.CC are more larger in diameter (?61cm) than the left in proportion (12:1).

Configuration of the tumour

Among the 5 Rt.CC 3 were exophytic and 2 were annular variety. Among the Lt.CC, most (19) were ulcerated variety followed by 8 exophytic and 2 annular tumour.

Gross extension of the tumour

Among the Rt.CC, 2 extended into the serous layer and 3 up to pericolic fat. On the other hand, 10 (29%) left sided tumours extended up to the serous coat followed by 7 tumours up to pericolic fat, 7 up to the whole thickness and another 6 up to muscle coat.

Histopathological diagnosis

Most of the tumours (30, 85.7%) were adenocarcinoma. among the 30 patients, 27 were left sided and only 3 were right sided. On the other hand 5 (14.3%) were mucinous adenocarcinoma of which 2 were right sided and 3 were left sided.

TNM classification of the tumour

Staging and grading of tumour

In case of staging, advance stage were more in right side in proportion to that of left (1.7:1). Maximum number (24, 69.6%) of Lt.CC were low grade and 6 (17.4%) were high grade tumour. On the other hand, 3 (8.6%) tumours were in high grade and 2 (5.7%) were in low grade on the right side. In case of grading, Rt.CC were more in high grade in proportion to that of the left side (3:1).This grading is done on the basis of CAP (Colleage of American Pathologists) protocol where well and moderately differentiated tumour are included into low grade and poorly, undifferentiated tumours were included into high grade.

Table II: Tumour staging and grading

Staging and grading	Right sided tumour	Left sided tumour	Total
Tumour staging			
Stage I	0	3(10%)	3(8.6%)
Stage II A	1(20%)	9(30%)	10(28.6%)
Stage II C	0	2(6.6%)	2(5.7%)
Stage III A	0	2(6.6%)	2(5.7%)
Stage III B	2(40%)	4(13.3%)	6(17.1%)
Stage III C	2(40%)	9(30%)	11(31.4%)
Stage IV	0	1(3.3%)	1(2.85%)
Total	5(100%)	30(100%)	35(100.0%)
Tumor grading			
High grade	3(60%)	6(20%)	9(25.7%)
Low grade	2(40%)	24(80%)	26(74.3%)
Total	5(100%)	30(100%)	35(100.0%)

Tumour infiltrative lymphocytes (TIL)

Maximum number (37%) was grade 2 TIL in case of Lt.CC followed by 9 in grade 1 and 8 in grade 3 . All five Rt.CC had grade 1 TIL cells.

Extracellular mucin

Maximum number of Lt.CC (17, 48.6%) had no extracellular mucin followed by 10 (29%) had 1-49% and only 3 had 50%. On the contrary, 2 Rt.CC had 50% and 3 had 1-49% extracellular mucin. Rt.CC were mostly associated with 50% extracellular mucin production than the left sided tumours (4:1).

Lymphatic, venous and perineural invasion of the tumours

Among the Rt.CC, only one case (2.9%) had all the 3 types of invasions like lymphatic, venous and perineural but on the other side 6 cases (17.4%) of

left sided tumours had all 3 type of invasion. Lymphatic invasion was the most common (3 right sided and 21 Lt.CC) followed by venous (2 right sided and 17 left sided) and perineural (1 right sided and 6 left sided tumours) invasion.

Circumferential margin

Circumferential margin of all the Rt.CC (5) was involved where as circumferential margin of 16 (46.4%) Lt.CC was involved but rest 14 (40%) had free margin.

Lymph node metastasis

In 34 cases, the resected specimen contains lymph node. Lymph node number varied from 1 to 34. Histologically, lymph node metastasis of CRCa were present in 21 cases. In the Rt.CC, 3 cases (60%) out of 5 cases showed lymph node metastasis. One case had no lymph node in resected specimen. On the other hand, 17 cases (56.6%) out of 30 cases of left side showed lymph node involvement.

Carcinoembryonic antigen (CEA)

Maximum number of patients (22, 62.9%) have normal level. Among the 13 (37%) patients with elevated CEA level (>5ng/ml), 11 (31.9%) were in the left and 2 (5.7%) were in the right side. Rt.CC had more elevated CEA level in proportion to that of the left (1.11:1).

Colonoscopy findings

Among the Rt.CC, colonoscopic findings showed 2 ulcero-proliferative, 1 ulcerated, 1 annular growth and report was unavailable in single case. In the left sided tumours, colonoscopy showed 10 ulcero-proliferative, 9 ulcerated, 3 annular, 2 polypoid growth and report was unavailable in 6 cases.

Discussion

CRCa is one of the most common malignant tumors in the developed as well as developing nations. Cancers arising from the Rt.CC differs significantly regarding epidemiological, clinical, histological and biological behavior from those in Lt.CC[8]. In Bangladesh no studies were done to see the clinical and morphological differences between the right sided and Lt.CC.

In this present study, the age ranges were from 14 years to 76 years with a mean age of 42.9 ± 13.7 years. Male and female ratio was 1.5:1. Keating *et al* (2003)[16] showed in his study that the male and female ratio was l.6: l. Fireman *et al* (2005)[17] showed female predominance in their study as among 624 cases 271 were male and 353 were female. Peak incidence of CRCa was between ages 40 -49 years which is lower than that of western and other developed countries. 71% of the cases were below the age of 50 years. Turner (2010)[1] found only 20% of the cases below 50 years. Keating et al (2003)[16] found only 6.3% cases below 50 years.

The mean age of CRCa in this present study indicate that CRCa is relatively common in lower age group in our country. Though CRCa is extremely rare in pediatric age group, a case of 14 years old girl was found in this study. Afroza *et al* (2007)[3] also reported a 11 years old Bangladeshi boy with primary mucinous adenocarcinoma in the rectum. These reflects incidence of CRCa in Bangladesh appears to be common in younger age group. This may be due to both environmental factors and genetic factors.

Benedix et al, (2010)[8] shows in Germany patients with Rt.CC were significantly older. In Greece, in a study also showed Rt.CC are more common in patients older than 60 years of age and in women (Christodoulidis et al[7], 2010) Rosai (2004)[4] also commented Rt.CC are more common in the elderly person.

In the present study, the mean age of the patient in the right side was 34.2 year with male to female ratio was 1: 1.5 and in the left side mean age was 44.3 years with male to female ratio 1.75:1. In this study Lt.CC patients were in older age group with male preponderance which was the reverse picture of the Beneedix[8], Christodoulidis[7] and Rosai[4] study. This age and sex variation may be due to geographical variation of diseases.

In this study, among the 35 respondents, maximum (30= 85.7%) had tumour on the left side and only 5 (14.3%) on the right side. Studies from Europe and Japan recently reported an increase in Rt.CC than the left side. In the US, where CRCa incidence has been declining, the rate of CRCa in right side is increasing.[22] Present study showed the occurrence of Lt.CC in Bangladesh gradually increasing.This rising trend of Lt.CC may be due to not adopting regular CRCa screening program, poor dietary habit and genetic abnormality.

Regarding the specific location, the Rt.CC were 2 (5.8%) each in caecum and transverse colon and 1 (2.9%) in right hepatic flexure. Lt.CC were mainly located in rectum (20= 58%). Raja (2010)[6] also showed distribution of colon cancer among 50 cases according to the site of the colon affected were as follows: 33 (66%) case were in rectum, 6 (12%) were in the ascending colon, 3 (6%) in hepatic flexure of colon, 2 (4%) each in caecum, descending colon, sigmoid colon and in the transverse colon. In Bangladesh CRCa mostly found in rectum that differs the Turner's study. Why in Bangladesh most of the CRCa occur in the rectum is not known that may be due to genetic cause.

Patients with Rt.CC present as fatigue, weakness, iron deficiency anemia and per rectal bleeding. Lt.CC come to attention by producing occult bleeding, changes in bowel habit or crampy left

lower quadrant discomfort. Chance for early discovery and successful removal should be greater for patients with lesions on the left side, because these patients usually have prominent disturbances in bowel functions such as melena, diarrhoea and constipation. Christodoulidis et al. (2010)[7] found that Rt.CC patients presented more with per rectal bleeding (64.01%) compared to Lt.CC patients (35.9%). On the contrary, symptoms associated with altered bowel habits and passage trouble were more common in patients with Lt.CC (36.89%) compared to right sided (23.88%). Nawa et al, (2008)[9] showed that symptoms associated with per rectal bleeding or anemia was significantly higher in patients with left- sided colon cancer than in those with right-sided colon cancer (61% vs. 48%). In contrast, symptoms associated with passage trouble or abdominal mass was significantly higher in patients with Rt.CC (35% vs. 27%). Benedix et al, (2010)[8] showed patients with Rt.CC have synchronous distant hepatic and pulmonary metastases and in Lt.CC have peritoneal metastases.

This study partly coincides the Nawa's study[9] and Turner's study[1] as because per rectal bleeding was the most common symptom in the left side (30=100%) compared to the right (2=40%). Abdominal pain (5=100%) was the commonest symptom in the right side compared to the left (6=20%). In the right a case was also presented with an abdominal lump (Table-I).

Regarding occupation, almost all the female patients were housewife and were 14 (40%) in number. Among the male patients, 9 (25.7%) were in service followed by 6 (17.1%) in business, 3 (8.6%) in agriculture, 2 (5.7%) were rickshaw puller and 1 (2.9%) was student. In this study a greater percentage of female were housewives having less physical activity comparatively. This may be an inciting event of having CRCa of these cases in our country.

In Japan where the incidence was previously very low rates have now risen to intermediate levels (similar to those in the United Kingdom), presumably as a result of changes in lifestyle and diet.[1] Increased BMI may be a contributory factor for the development of CRCa in our country.

A diet that is high in red meats (beef, pork, lamb) and processed meats (hot dogs and some luncheon meats) can increase CRCa risk. Epidemiologic studies have indicated that red meat consumption is strongly associated with colon cancer[23].

In the present study, Patients having Lt.CC took more meat than the Rt.CC (Left, 3-4 times/m, 11=36.6% vs. right, 3-4 times /month, 1=20%). In our country intake of red meat (beef) may be an important contributory factor for the development of colon cancer.

First degree relatives of people with CRCa have 2 to 3 fold increased risk of CRCa[24]. In present study maximum number (28) of patients did not have a positive family history and only 7 (20%) had history of different types of malignancy in their family members. Respondents having Lt.CC had positive family history same in proportion to that of Rt.CC (1:1).In our country the possible cause of having the positive family history may be because of inherited genes shared environmental factors, or some combination of these.

In present study mean diameter of the Rt.CC was 40.4 cm and in the left was 21.69 cm. Rt.CC were larger in diameter than the left.This observation is similar to the study done by Christodoulidis et al (2010)[7] and Hiroshi et al (2000)[11].

In present study Rt.CC were mostly exophytic (3=60%) compared to left (8=26.6%). Lt.CC were mostly ulcerating type (19=54.3%).Tumors in the proximal colon (right) tends to grow as exophytic masses that extends along one wall of the capacious caecum and ascending colon, Whereas carcinoma in the distal colon (left) tends to be annular, endophytic encircling lesions that produce napkin-ring constriction of the wall.[1] This present study correlates with the Turner[1] study.

Nawa et al, (2008)[9] found in his study exophytic type cancer was more prevalent in the left colon than in the right colon (59% vs. 40%). In contrast, the proportion of flat type cancer in the right colon was significantly higher than that in the left colon (left 25% ; right 44 %). This dynamic variation of tumor configuration may be explained on genetic background.

Benedix et al (2010)[8] showed Rt.CC are locally advanced cancer than the left and have a worse prognosis. Present study showed extension of Rt.CC up to pericolic fat were more (3=60%) compared to that of left side (7=23.3%) which correlates with the Benedix's study[8].

Almost all the 5 Rt.CC showed proximal dilatation to the tumor. Among the left, 14 had full dilatation changes followed by 9 had no change and 7 had mild dilatation. Grossly the Rt.CC were mostly exophytic type and theoretically there should be dilatation proximal to the tumor. The present study also correlates the gross feature of the tumor.

On histological examination of 35 CRCa cases, 30 (85.7%) cases were adenocarcinoma (NOS) and five (12%) cases were mucinous adenocarcinoma. Among these 30 cases of adenocarcinoma 27 were left sided and only three were right sided. Of the five (14.3%) mucinous adenocarcinoma two were right sided and three were left sided. Among the three adenocarcinoma on right side, one had moderate differentiation with mild papillary changes, one had moderate differentiation with

moderate papillary changes and one had poorly differentiation. Among the 27 adenocarcinoma on the left side, 10 were moderately differentiated, four were moderately differentiated with mild papillary changes, seven (one with clear cell change) were moderately differentiated with moderate papillary changes, four (one with clear cell change) were moderately differentiated with pronounced papillary changes and rest two were poorly differentiated. No well differentiated cancer was reported in this series. Most of the colon cancer is adenocarcinoma, (30=85.7%) observed in my study. This finding is similar to the findings described by Yaw et al, (2007)[25] (84.16%), Raja(2010)[6] (88%), Hossain(2007)[5] (74%), Keating et al (2003)[16] (94.7%) and Pahlavan et al(2006)[26] (90%).

In present study poorly differentiated adenocarcinoma (1=20% vs. 2=6.6%) and mucinous adenocarcinoma (2=40% vs. 3=10%) was found more on right side compared to the left.

Tendency of Rt.CC to be less differentiated such as poorly differentiated adenocarcinoma, signet ring cell carcinoma and mucinous carcinoma is similar to the observation stated by (Hiroshi et al,[11], Nawa et al,[9], Keating et al,[16] Raja,[6])

The major role of proper staging of CRCa, provide the information to physician regarding patient's prognosis and the need for adjuvant therapy. For many years, pathologists used the classic Dukes' classification (1932), Astler-Coller classification (1954) and the TNM classification[1] (Table-II). According to TNM classification staging of tumor was done in my study. In this study Rt.CC had a higher stage of disease than the left (T2N1MX, right 40% vs. left 16.6%) which reflects the poor prognosis of patients with right colon cancer. This observation is similar to the studies done by Benedix et al,[8] Nawa et at,[9]).

Ropponem et al,(1997)[27] shows that colonic cancer patients having many tumour infiltrative lymphocytes (TILs) tend to have a better prognosis than those with few tumour infiltrative lymphocytes. Lt.CC patients have a statistically significant better overall survival rate compared to right side[7]. In present study regarding grading of TIL Lt.CC showed higher grade. All (five) Rt.CC (5=100%) had grade 1 TIL with 2 cases in stage IIIC, 2 in IIIB, and 1 were in stage IIA. On the left side maximum were in grade 2 and grade 3 TILs with 10 cases in stage IIIC, four in IIIB , two in IIIA, two in IIC, nine in IIA and three in stage I. It shows lower TIL is associated with higher stage though conclusion cannot be made from this small sample size. This findings also coincide with other studies and adding points to Rt.CC to have an worse prognosis.

In Rt.CC and in younger patients the percentage of mucin secreting adenocarcinomawas significantly higher[12]. In the present study Rt.CC were mostly associated with (50%) extracellular mucin production than the Lt.CC (4:1) which also follow the previous study.

Ekem et al (2008)[28] found lymphovascular invasion in 33% cases. Raja (2010)[6] found in his study lymphovascular invasion was present in 16(32%) cases and absent in 34 (68%) cases. Out of 16 positive cases 12(75%%) cases had stage III disease and 3(19%) cases had stage II and one (6%) case in stage IV disease, which indicates higher stage disease in lymphovascular invasion positive tumour. In this study, majority of the cases in stage III disease show lymphovascular invasion.

In present study lymphatic invasion was found more (21=70%) in left side compared to the right (3=60%). Vascular invasion was also more (17=56.6%) in left side compared to the right (2=40%) and perineural invasion were same in both side.

In this study, majority of the cases in stage IIIC disease show lymphovascular invasion.This partly explains the importance of reporting lymphovascular invasion and Tumor infiltrating lymphocytes in surgical pathology report.Vascular invasion reduces the survival rate 5 years and extramural vascular invasion is worse than invasion within the bowel wall[4].

Tumours with pushing margin and inflammatory cells (eosinophil and plasma cells) have a better prognosis[4]. In this study Rt.CC had more infiltrative border than the left in proportion (1.07:1) that reflect worse prognostic feature of the Rt.CC.

Tumours associated with involved circumferential margin have a poorer prognosis and local recurrence[4]. Circumferential margin of all the Rt.CC (5=100%) were involved compared to the left (16=53.3%) . This finding also denotes the poor prognostic evidence of Rt.CC.

Present study showed advance stage tumor (stage IIIC=40%) were more in right side compared to left side (stage IIIC=33.3%). Rt.CC patients had an advanced stage at the time of diagnosis compared to the left indicates aggressive behavior of the Rt.CC with worse prognosis. In Raja's (2010)[6] study maximum number of cases 22 (44%) were in stage III, 14 (28%) were in stage II and 13 (26%) in stage I and one (2%) in stage IV. Derwinger et al (2010)[29] found 41% cases in stage III, 36% cases in stage II, 12% cases in stage IV and 10% cases in stage I.

Rt.CC were more in high grade (3=60%) compared to that of left side (6=17.4%).This indicate patients with Rt.CC diagnosed lately. This

may be due to negligence of the patients of attending to physician lately or unawareness of regarding regular CRCa screening program.

Rt.CC cases were more in number with elevated CEA level and with advanced stage (stage IIIB 50% vs. 18%) compared to the left. However large scale study is required to find out a fair relation regarding of elevated CEA level with stage. Rosai (2004) commented CEA level more than 5 ng/ml as the adverse prognosis factor in CRCa. In Raja's study[6], in 25 cases having CEA more than 5 ng/ml, 17(68%) cases were in stage III and 1 case was in stage I. This shows majority of the patients having elevated CEA are in high stage disease. Aljebreen (2007)[30] found 32% of cases of CRCa with elevated CEA level.

Cases with nodal metastasis in Rt.CC (3=75%) were more compared to the left side (17=56.6%). In the Rt.CC, among the 3 cases with nodal metastasis, 1 were mucinous adenocarcinoma, 1 were poorly differentiated adenocarcinoma and 1 with moderately differentiated adenocarcinoma. In the Lt.CC, among the 17 cases with nodal metastasis in Lt.CC 3cases were mucinous adenocarcinoma, 3 were poorly differentiated adenocarcinoma, and 15 were moderately differentiated adenocarcinoma. The patients with Rt.CC have a higher prevalence of distant lymph node metastasis with poorly differentiation compared (33.35% vs. 18%) to the Lt.CC. It indicates patients are in advanced stage at the time of attending physician.

In Raja's study[6], 49 colon cancer specimens were accompanied by lymph nodes. Of these 23(47%) had nodal metastasis. It indicates patients are in advanced stage at the time of attending physician. In 23 nodal metastasis cases 17(74%) were moderately differentiated and 6(26%) cases were poorly differentiated tumor. The greater the lymph node involved the worse the prognosis. If 6 lymph node shows metastasis, less than 10% of the patient survived more than 5 years. If more than 16 lymph node show metastasis, all patient die within 5 years[4]. The patients with Rt.CC have a higher prevalence of distant lymph node involvement and peritoneal metastasis, than those with Lt.CC.[11] The present study correlates the above mentioned study.

Colonoscopically, Ulcero-proliferative and annular lesion were more in right side (2=40%, 1=20%) compared to that of left side (10=33.3%, 3=10%). Ulcerated lesion was more in left side (9=30%) compared to that of right side (1=20%). In the left side two polypoid lesions was also found. Grossly regarding the tumor configuration ulcerating type was more in the left side and exophytic type was more in the right side that correlates with the colonoscopic findings in this study.

Conclusion:

Rt.CC are characterized as a distinct entity due to specific age distribution, female prevalence, larger diameter, poor differentiation, association with mucinous adenocarcinoma, more advance stage and higher grade. Further in-depth analysis with larger number of cases would provide light to find out the discrepancies between right and left sided colon cancers and molecular genomic alterations involved in CRCa.

Referance:

1. Turner JR. 'The Gastrointestinal Tract' in Robbins and Cotran Pathologic Basis of Disease, 8th edition, Kumar, V. Abbas, A.K. Fausto, N and Aster, J. C . W B Saunders company, Philadelphia, Pennsylvania, 2010, 822-825.

2. Korean Statistical Informative Service, 2005.

3. Afroza A, Hasan S, Rukunuzzaman M, Hussain SA, Amin R. Carcinoma Rectum in an 11 Years old Boy. Mymensingh Medical Journal, 2007; 16: 70- 72.

4. Rosai J.(ed) 'Gastrointestinal tract' in Ackerman's Surgical Pathology. 9th edition, Mosby Company, St Luis, 2004; 1:776-825.

5. Hossain T. 'Clinicopathological study of CRCa'. MD Thesis, Bangabandhu Sheikh Mujib Medical University, Dhaka 2007.

6. Raza AK. 'Clinopathologic pattern and DNA methylation status of CRCa in a group of Bangladeshi population. M.phil Thesis, Bangabandhu SheikhMujibMedical University, 2010.

7. Christodoulidis G, Spyridakis M, Symeonidis D, Kapatou A, Monolakis A, Tepetes K. 'Clinicopathological differences between-right- and left –sided colonic tumours and impact upon survival' Tech Coloproctol, 2110; 14 : 45-47.

8. Benedix F, Kube R, Meyer F, Schmidt U, Gastinger I, Lippert H. 'comparison of 17,641 patients with right and Lt.CC: differences in epidemiology, perioperative course, histology and survival', Dis Colon Rectum 2010; 53 : 57-64.

9. Nawa T, Kato J, Kawamoto H, Okada H, Yamamoto H, Kohno H, Endo H, Shiratori Y. 'Differences between right- and Lt.CC in patient characteristics, cancer morphology and histology'.Journal of Gastroenterology and Hepatology 2008; 23: 418-423

10. Suttie SA, Shaikh I, Mullen R, Amin AI, Daniel T, Yalamarthi S. Outcome of right and left sided colonic and rectal cancer following surgical resection**.** The Association of Coloproctology of

Great Britain and Ireland, 2010;10: 1463-1318.

11. Hiroshi K, Masao T, Junji O, Ichizo W, Tetsuhisa Y, Keitaro T, Toshiyuki T, Nobuhiko T. 'Clinicopathological differences between Right-sided and Left –sided Colon Cancer', Journal of Japan Surgical association 2000;61(4):846-851.

12. Zivkovic V, Katic V, Dordovic B, Krstic M, Pejovic S, Petrovic A, Fakultet M, Patologiju, Srbija N. 'Clinicopathological Characteristics of colonic carcinoma in relation to localization and histologic type'. Vojnosanit Pregl, 2007; 64: 827-831.

13. Snaebjornsson P, Jonasson L, Jonsson T, Moller PH, Theodors A, Jonasson JG. Colon cancer in Iceland—A nationwide comparative study on various pathology parameters with respect to right and left tumor location and patients age. International journal of cancer 2010; 127(11): 2645-2653.

14. Sugai T, Habano W, Jiao Y F, Tsukahara M, Takeda Y, Tsuka KO, Nakamura S. Analysis of Molecular Alteration in left – and right sided CRCas reveals distinct pathways of carcinogenesis. Journal of Molecular Diagnostics, 2006; 8: 193-201.

15. Jiang LX, Xu J, Wang Z, Li DP, Peng ZH, Gao JJ, He I, Zheng HT. 'Tumor suppress genes screening analysis on 4q in sporadic CRCa'.World J, Gastroenterol 2008; 14: 5606-5611.

16. Keating J, Pater P, Lolohea S, Wickremesekera K. 'The epidemiology of CRCa: what can we learn from the New Zealand Cancer Registry'. The New Zealand Medical Journal 2003;116: 1-8.

17. Fireman Z, Neiman E, Mouch SA, Kopelman Y. 'Trends in incidence of CRCa in Jewish and Arab population in central Israel', Digestion 2005;72: 223-227.

18. Gomez D, Dalai Z, Raw E, Roberts C, Lyndon PJ. 'Anatomical distribution of CRCa over 10 years period in a district general hospital: is there a true rightward shift?',Postgraduate Medical Journal 2004;80: 667-669.

19. Riddell RH, Petras RE, Williams GT, Sobin LH. 'Epithelial neoplasia of the intestines' in Tumors of the Intestines. Third series,Fascicle 32, Armed forces institute of pathology,Washington,DC, 2003; 85-240.

20. Leon MPD, Marino M, Benatti P, Rossi G, Menegatti M, Pedron M, Gregorio CD, Losi L, Borghi F, Scarsclli A, Ponti G, Roncari B, Zangardi G, Abbati G, Ascari E, Roncucci L. ' Trend of incidence, sub site distribution and staging of colorectal neoplasms in the 15-year experience of a specialized cancer registry'. Annals of Oncology 2004;15: 940-946.

21. Ayyub MI, Alradi AO, Khazeinder AM, Nagi AH, Maniyar IA. 'Clinicopathological trends in CRCa in a tertiary care hospital'. Saudi Medical Journal 2002; 23:160-163.

22. Wray CM, Ziogas A, Hinojosa MW, Le H, Stamos MJ, Zell JA. 'Tumor subsite location within the colon is prognostic for survival after colon cancer diagnosis' Dis Colon Rectum, 2009; 52: 1359-1366.

23. Hamilton SR, Vogelstein B, Kudo S, Riboli E, Nakamura S, Hainaut P, Rubio CA, Sobin LH, Fogt F, Winawer SJ, Goldgar DE, Jass JR. 'Carcinoma of the colon and rectum' in Pathology and Genetics of Tumour of the Digestive System,Hamilton S.R. and Aaltonen, L. A, IARC press, Lyon, France 2000; 103-142.

24. Atlanta GA. Cancer Facts & Figures. American Cancer Society 2011.

25. Yaw KT, Bakari AA, Pindiga UH, Mayun AA. 'Clinicopathological pattern and challenges in the management of CRCa in sub-SaharAfrica'. Journal of Chinese Clinical Medicine, 2007: 2: 688-694.

26. Pahlavan PS, Khantan R. ´The Epidemiology and Clinical findings of CRCa in Iran'. J Gastrointest Liver Dis 2006; 15:15-19.

27. Ropponen KM, Eskelenen MJ, Lipponen PK, Alhava E, Kosma VM. 'Prognostic Value of Tumour Infiltrating Lymphocytes (TIL) in CRCa'.Journal of Pathology 1997; 182: 318-324.

28. Ekem TE, Bahadir B, Gun BD, Bektas S, Kertis G, Yurdakan G, Ozdamar SO. 'CRCas: Clinicopathologic investigation, correlation with expression of estrogen and progesterone receptors', Turkish Journal of Cancer 2008;38:118-122.

29. Derwinger K, Kodeda K, Bexe-Lindskog E, Taflin H. 'Tumour differentiation grade is associated with TNM staging and the risk of node metastasis in CRCa', Acta Oncologica 2010; 49: 57–62.

30. Aljebreen AM. 'Clinico-Pathological Patterns of CRCa in Saudi Arabia.2007.