Clinico-Epidemiology Study of Colorectal Cancer in Menofia University Oncology Department

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Abstract: Purpose: Colorectal cancer (CRC) is the most common malignancy of the gastrointestinal tract and is the third most common cancer worldwide after lung and breast cancers**,** CRC was the 6th cancer in Egypt. This work was designed to study patient and disease characteristics, medical treatment option and response of all colorectal cancer patients presented in Menofiaoncology department between 2005 and 2010. **Methods:** in this retrospective study, we analyzed the clinical reports of all patients who had a clinical and histopathological diagnosis of colon and rectal cancer presented to Menofia university clinical oncology department, between March 2005 till December 2010. **Results:** 84 patients admitted to oncology department from 2005 to 2010 patients with overall incidence about 1.6% of all patients admitted to Menofiaoncology department. Of these, 47 patients (56%) were diagnosed by colon cancer (group 1) and 37(44%) patients were diagnosed by rectal cancer (group 2). 35.7% (30 patients) were less than 50 years. The median age at diagnosis for colon cancer (group 1) patients was 49 years old and for rectal cancer group (group 2) was 52 years. There was male predominance.poor performance status, advanced stage, presence of metastases and elevated CA 19.9 are associated with poor survival in colon cancer group and advanced stage and disease progression at initial response in rectal cancer group. **Conclusion:** colon cancer is more common than rectalcancer, with clear male predominance. It is frequent in patients less than 50 years and urban than rural areas. Patients with colon cancer have better overall survival than rectal cancer. Advanced stage, presence of metastases and elevated CA 19.9 are associated with poor survival in colon cancer group and advanced stage and disease progression at initial response in rectal cancer group.
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1. Introduction:

Colorectal cancer (CRC) is the third most common cancer worldwide after lung and breast cancers with two-thirds of all colorectal cancers occurring in the more developed regions of the world. CRC affects men and women of all racial and ethnic groups, and is most often found in those aged 50 years or older. Colonoscopy plays a central role in the detection and prevention of CRC[1]**.**

In the United States, both the incidence and mortality have been slowly but steadily decreasing. Annually approximately 132,700 new cases of large bowel cancer are diagnosed, of which 93,090 are colon and the remainder rectal cancers[2]

CRC was the 6th cancer in Egypt, representing 4% of the total cancers and 53% of GIT cancers. The median age was 53 years with male predominance. Colon cancers were more common than rectal cancers[3].

Most colorectal cancer occurs due to life style and increasing age with only a minority of cases associated with underlying genetic disorders. It typically starts in the lining of the bowel and if left untreated, can grow into the muscle layers underneath, and then through the bowel wall. Screening is effective at decreasing the chance of dying from colorectal cancer and is recommended starting at the age of 50 and continuing until a person is 75 years old. Localized bowel cancer is usually diagnosed through sigmoidoscopy or colonoscopy[4].

There are several modifiable risk factors for colorectal cancer and building predictive models encompassing both genetic and environmental factors enables us to move in the direction of a complete assessment of disease risk[5]**.**

Symptoms of colorectal cancer typically include rectal bleeding and anemia which are sometimes associated with weight loss and changes in bowel habits[6]. Due to epidemiological burden of the disease this study was carried out

Aim of the work:

Study patient and disease characteristics, medical treatment option and response of all colorectal cancer patients presented in Menofiaoncology department between 2005 and 2010.

2. Materials and methods:

We included in this retrospective study, the clinical reports of all patients who had a clinical andhistopathological diagnosis of colon and rectal

cancer presented to Menofia university clinical oncology department, between March 2005 till December 2010. We excluded patients having history of other malignancy, Data collected and tabulated in descriptive and analytic tables statistical comparison was performed according to SPSS (Statistical Package for Social Science) version 16.

The variables that were analyzed included, age, gender, residence, body mass index (BMI), performance status, presenting symptoms, Response to treatment was assessed according to revised RECIST guide line[7] (version 1.1).

Tests used in analysis were person chi. Square test and fisher's exact test. They were used to determine the significance of associations between categorical variables and response. Survival was analyzed using the Kaplan–Meier curve. It was calculated from the date of diagnosis to the date of progression or the date death (all causes) which ever occur first, patients who were not progressed at last follow up were censored.

Differences between groups were assessed by means of the log-rank test.

Two-sided p-value <0.05 was considered statically significant.

3. Results:

We analyzed the medical records of 84 patients admitted to oncology department from 2005 to 2010 patients. Of these, 47 patients (56%) were diagnosed by colon cancer (group 1) and 37(44%) patients were diagnosed by rectal cancer (group 2). patients characteristics are shown in table (1).

As regard patients with colon cancer patients (group 1), 21(44.7%) patients aged less than 50 years, and male to female ratio was 2:1. Colon cancer was more common in rural than urban areas. Abdominal pain and intestinal obstruction were the most common presentations.

While in rectal cancer patients (group 2), 28 (75.7%) patients of them aged more than 50 years, and male to female ratio were 2:1rectal cancer was more common in urban areas. bleeding per rectum followed by abdominal pain were the most frequent presenting symptoms. bleeding per rectum followed by abdominal pain were the most frequent presenting symptoms.

As regard disease characteristics (table 2), in group 1 (colon cancer patients), descending colon was the most common site for tumor and adenocarcinoma was the most common histology.T3 and N2 disease were the most frequent and 23 patients (48.9%) were metastatic at presentation with 9 patients (39.1%) with multiple metastatic sites and liver was the most common metastatic site. In group 2 (rectal cancer patients), lower rectal presentation was the most common, T3 and N2 were the most common presentation

Table (1) personal characteristics:

Personal data	Colon (N=47)		Rectum (N=37)	
	No.	%	No.	%
Age / years				
<50	**21**	**44.7**	**9**	**24.3**
≥50	**26**	**55.3**	**28**	**75.7**
Gender:				
Male	**31**	**66**	**25**	**67.6**
Female	**16**	**34**	**12**	**32.4**
Smoking :				
Yes	**16**	**34**	**20**	**54.1**
No	**31**	**66**	**17**	**45.9**
Residence:				
Urban	**25**	**53.2**	**26**	**70.3**
Rural	**22**	**46.8**	**11**	**29.7**
BMI:				
<25	**26**	**55.3**	**11**	**29.7**
≥25	**21**	**44.7**	**26**	**70.3**
Performance state:				
0	**26**	**55.3**	**17**	**35.1**
1	**17**	**36.2**	**17**	**45.9**
2	**4**	**8.5**	**7**	**18.9**
Associated co morbidities:				
No	**35**	**74.5**	**27**	**73**
Diabetes mellitus	**4**	**8.5**	**3**	**8.1**
Hypertension	**2**	**4.3**	**3**	**8.1**
Liver cirrhosis	**5**	**10.6**	**2**	**5.4**
COPD	**1**	**2.1**	**2**	**5.4**
Presenting symptoms:				
Abdominal pain	**16**	**34**	**13**	**35.1**
Constipation	**6**	**12.8**	**3**	**8.1**
Bleeding per rectum	**8**	**17**	**14**	**37.8**
Diarrhea	**3**	**6.4**	**1**	**2,7**
Intestinal obstruction	**14**	**29.8**	**6**	**16.2**

Disease characteristics are shown in table (2).

Table (2). Disease characteristics

Tumor characters		Colon(N=47)		Rectum(N=37)	
		No	%	No	%
Site:		**ascending:** 8 **descending:** 32 **Transverse:** 7	17 68.1 14.9	**Upper**: 18 **Lower:** 19	48.6 51.4
Histopathology: - Adenocarcinoma - Undifferentiated		43 4	91.5 8.5	34 3	91.9 8.1
Stage (TNM)	- T1 - T2 - T3 - T4	3 9 27 8	6.4 19.1 57.4 17	2 12 15 8	5.4 32.4 40.5 21.6
	- N0 - N1 - N2	12 14 21	25.5 29.8 44.7	7 14 16	18.9 37.8 43.2
	- M0 - M1	24 23	51.1 48.9	26 11	70.3 29.7
Site of metastasis: - Single - Multiple		14 9	60.9 39.1	8 3	72.7 27.3
Initial tumor marker **CEA** - Elevated - Not elevated **CA19-9** - Elevated - Not elevated		 16 31 13 34	 66 34 27.7 72.3	 9 28 7 30	 24.3 75.7 18.9 81.1
Treatment - Chemotherapy - Surgery +chemotherapy - Concomitant chemo radiotherapy + surgery		24 23 0	51.1 48.9 0	11 0 26	29.7 0 70.3
Response to treatment - Complete response (CR) - Partial response (PR) - Stable disease (SD) - progress		23 8 6 10	48.9 17 12.8 21.3	12 9 3 13	32.4 24.3 8.1 35.1

As regard survival in group 1 (patients with colon cancer) (table 3) there was significant correlation between survival and patient performance status with best survival in patient with performance status 0 (20.15 months), also patients with no comorbidities has better survival (19.6 months) than those with comorbid illness.

Patients with T1disease and no metastases has better survival than others and patients with initially elevated CA19.9 has worse survival then patients with normal CA19.9.

Table (3) shows probability of living in cancer colon group (group 1)

Colon cancer		Overall survival Mean (95% CI)	SE	Log rank	P value
Age /years	<50 ≥50	17.09 (11.1 - 22.9) 18.15 (12.2 - 24.0)	3.012 3.016	0.111	0.739
Gender:	Male Female	15.93 (10.9 - 20.97) 21.06 (13.7 - 28.35)	2.56 3.72	1.930	0.165
Smoking :	Yes No	16.55 (11.74 - 21.36) 19.20 (11.79 - 26.60)	2.45 3.77	0.311	0.577
Residence:	Urban Rural	15.31 (9.08 - 21.55) 19.76 (14.2 - 25.32)	3.18 2.83	1.427	0.232
BMI	<25 ≥25	19.81 (12.42 - 27.19) 15.96 (11.34 - 20.57)	3.76 2.35	0.951	0.329
Performance state:	0 1 2	20.15 (13.07 - 27.23) 15.88 (12.61 - 19.14) 9.25 (8.31 - 10.18)	3.61 1.66 0.47	6.428	0.040(S)
Associated co morbidities:	No D.M HTN Liver cirrhosis COPD	19.6 (14.3 - 24.89) 11.75 (9.43 -14.06) 9.50 (8.52 - 10.48) 14.2 (4.93 - 4.53) 8.0 (8.00 - 21.84)	2.70 1.18 0.50 4.93 0.00	10.63	0.031(S)
Stage (TNM):	T1 T2 T3 T4	38.17(11.82 - 46.0) 31.7 (22.14 - 37.4) 12.1(10.26 -13.95) 10.0 (8.1 - 11.81)	17.43 4.91 0.94 0.92	28.60	0.001(S)
	N0 N1 N2	25.09 (12.93 - 37.24) 15.93 (11.57 - 20.29) 12.2 (9.26 - 15.13)	6.20 2.22 1.49	3.359	0.187
	M0 M1	23.12 (16.12 - 30.13) 12.0 (8.94 - 15.05)	3.57 1.56	10.10	0.001(S)
Site of metastasis:	Single Multiple	15.22(8.34 – 22.09) 12.92(8.46 – 17.39)	3.50 2.27	0.777	0.378
CEA	Elevated Not elevated	13.62 (9.46 - 17.78) 19.77 (13.93 - 25.61)	2.12 2.98	2.24	0.134
CA19-9	Elevated Not elevated	11.15 (8.19 - 14.11) 20.17 (14.74 - 25.6)	1.51 2.77	7.04	0.008(S)
Response to treatment	CR PR SD Progress	26.82(24.42 – 29.22) 16.75(13.81 – 19.68) 9.33(7.39 – 11.27) 8.40(6.57 – 10.22)	1.22 1.49 0.98 0.93	63.14	0.001
Histopathology	Adenocarcinoma Undifferentiated	17.93(13.44 - 22.41) 15.0 (5.98 - 24.01)	2.28 4.60	0.183	0.669

Stage, presence of metastases and initial treatment response were the independent risk factors.

Multivariate cox regression analysis for colon cancer group are shown in table (4).

Table (4) Multivariate cox regression analysis for colon cancer group

Variable	WALD	Hazard ratio	P value	CI 95%	
				Lower	Upper
Stage	23.21	3.81	0.001(HS)	2.214	6.586
Metastasis	10.08	3.33	0.001(HS)	1.586	7.006
CA19-9	3.64	1.97	0.056	0.982	3.980
Performance state	0.39	0.83	0.530	0.477	1.464
Associated co morbidity	0.01	1.01	0.918	0.804	1.274
Response to treatment	39.34	3.60	0.001(HS)	2.413	5.375

As regard group 2 (rectal cancer) there is significant correlation between tumor stage and initial response and overall survival. Also well differentiated tumors and patients who respond early to treatment had better survival.

Table (5) for probability of living for rectal cancer group

Rectal cancer		Overall survival Mean (95% CI)	SE	Log rank	P value
Age /years	<50 ≥50	31.22 (13.57 - 38.87) 23.60 (16.17 - 31.04)	24.31 3.79	0.998	0.318
Gender:	Male Female	35.92 (17.51 - 37.32) 18.66 (8.82 - 28.50)	9.38 5.02	2.654	0.103
Smoking :	Yes No	21.88 (12.27 - 31.49) 37.50 (15.05 - 38.94)	4.90 11.45	1.394	0.238
Residence:	Urban Rural	30.23 (12.92 - 36.53) 30.54 (13.88 - 34.20)	8.83 8.49	0.110	0.740
BMI	<25 ≥25	33.61 (15.86 - 38.36) 22.54 (10.20 - 34.88)	9.05 6.29	0.634	0.426
Performance state:	0 1 2	25.38 (13.12 - 37.64) 27.88(17.20 - 38.56) 45.42 (9.00 - 10.7)	6.25 5.44 31.7	0.013	0.994
Associated co morbidities:	No D.M HTN Liver cirrhosis COPD	34.74 (17.26 - 37.21) 31.00 (21.2 - 33.8) 12.66 (11.36 - 13.97) 13.0 (7.12 - 18.88) 13.0 (10.56 - 16.44)	8.91 5.00 0.66 3.00 1.50	4.739	0.315
Stage (TNM):	T1 T2 T3 T4	59 (24.99 - 93.00) 49.5 (0.00 - 99.48) 15.53 (12.73 - 18.33) 10.25 (8.16 - 12.33)	17.34 25.50 1.42 1.06	33.759	0.001(S)
	N0 N1 N2	62.42 (1.85 - 38) 30.18 (19.49 - 37.88) 14.42 (10.83 -18.02)	30.9 5.45 1.83	9.822	0.007(S)
	M0 M1	36.80 (18.91 - 54.7) 15.0 (9.84 - 20.15)	9.13 2.63	5.530	0.019(S)
Site of metastasis:	Single Multiple	18.66(7.27 – 30.05) 11.00(7.60 – 14.39)	5.81 1.73	1.989	0.158
CEA	Elevated Not elevated	19.22 (6.10 - 32.33) 33.86 (17.33 - 38.44)	6.69 8.44	2.268	0.132
CA19-9	Elevated Not elevated	16.42 (9.95 - 22.89) 33.56 (17.77 - 37.36)	3.30 8.05	1.30	0.254
Response to treatment	CR PR SD Progress	24(19.82 – 28.17) 13.5(10.06 – 17.04) 11.3(7.69 – 14.97) 6.46(4.86 – 8.05)	2.13 1.78 1.85 0.81	44.739	0.001(S)
Histopathology	Adenocarcinoma Undifferentiated	31.97 (17.94 - 36.0) 11.66 (11.01 - 12.32)	7.15 0.33	3.751	0.053(S)

Tumor stage, presence of metastases and initial response to treatment were the most independent factors for recurrence.

Table (6) shows multivariate cox regression analysis for rectal carcinoma group

Variable	WALD	Hazard ratio	P value	CI 95%	
				Lower	Upper
Stage	22.19	5.747	0.001(HS)	2.776	11.895
L.N	1.421	1.509	0.233	0.767	2.968
Metastasis	7.395	3.337	0.007(HS)	1.400	7.952
Response to treatment	28.47	3.430	0.001(HS)	2.181	5.395
Histopathology	0.006	0.948	0.938	0.248	3.623

4. Discussion:

Colorectal cancer is a major cause of morbidity and mortality thorough the world with large geographicaldifferences[8].

Colorectal cancer in Egypt, like most of the developing countries, is lower than that of developed countries with western lifestyle[3].

In Egypt, it is the 6th ranked cancer representing about 4% of total cancers in both sexes compared to the 3rd rank and about 11% for USA[9].

Variation in environmental risk factors particularly the higher content of dietary fibers, more physical activity and lower obesity rates can explain for the different incidence rates[3].

In Egypt, the median age for CRC is more than a decade earlier than that in the developing countries like USA. As shown in countries is much higher reaching up to 62% in USA[10]**.**

Over 6 years from 2005 to 2010 a total of 92 patients were diagnosed with CRC by colonoscopy; with overall incidence about 1.6% of all patients admitted to Menofia oncology department. of these patients, 8 were excluded because of incomplete data or lack of follow-up shortly after diagnosis.so, The study was carried out on 84patient divided into two group 47patient colon cancer(group 1) and 37patient rectum cancer(group 2).

This number is lower than that recorded at national cancer institute in Egypt at 2001 where **(Elattar, et al., 2002)** reported total number of 361 patients representing 3.7% of all cancer cases[11].

Also this number is much lower than that recorded by **(Veruttipong et al., 2012)** who reported in the registry for the period of (1999-2007), 1364 patients diagnosed in Gharbiah [12].

Sibiani et al., 2011 reported that In January 2005 to December 2009, 192 patients were diagnosed with CRC by colonoscopy; at King Abdul Aziz University Hospital in Jeddah, Saudi Arabia[13], although it is considered as low incidence country.

However this low number of patients is nearly the same like this reported by **Aljebreen 2007** who reported a total of 113 patients were included over the 10 year period in Saudi Arabia [14].This low incidence in our study is mainly due to bad filing and recording system in our department.

As regard age in our study 35.7% (30 patients) were less than 50 years, 21patients in group 1 and 9 patients in group 2. This goes with the results of **Aljebreen, 2007** who reported 37% percent of total 113 patients were 50 years of age or younger[14]. Also these results goes with that of **Mansoor et al., 2002** reported that 39% of their patients were below 50 years[15.]

This high incidence in younger age group may suggest hidden genetic element which needs more investigations. Also **Sibiani et al., 2011** reported that Approximately one third of all patients included in their study(50 patients out of 177 patients) were younger than 50 years old [13].

Veruttipong et al.,2012 reported that 22.0% of all cases were under the age of 40 in Gharbiah in Egypt[12]. While, in our study there 24 patients aged less than 40 years(about 28.5%) of all of our patients.

The median age at diagnosis for colon cancer (group 1) patients was 49 years old and for rectal cancer group (group 2) was 52 years this is nearly the same like that reported by **Elattar, et al., 2002** who reported median age at diagnosis 48 years for both males and females in patients of National cancer institute in Cairo,Egypt[11].

Also the median age of patients analyzed in our study is lower than that reported by**Aljebreen, 2007** in Saudi Arabia which was 55 years old[14].

This high incidence in young age may be due to pollution or different life style or diet habits in new generations. Or may suggest a hidden genetic element that should be investigated.

In our study both colon and rectal cancer were more common in urban (60.7%) (25 patients in colon

cancer group and 26 patients in rectal cancer group) than rural (39.3%) areas and this goes with **(Veruttipong et al., 2012)** who found that Colorectal cancer was more common in patients from urban (55%) than rural (45%) areas in Gharbiah in Egypt[12]. This is expected because of different dietary habits which depend on fat and fast foods in urban areas and more vegetables in rural areas and different life style.

In our study male to female ratio was1.9:1 for colon cancer group and 2:1for rectal cancer group these results go with that of **(Veruttipong et al., 2012)** who recorded male predominance (1.3:1) in Gharbiah in Egypt[12].and this is expected due more exposure of males to pollution and diet risk factors and higher incidence of smoking.

These results are in contrast to **Santos et al., 2008**showed higher incidence of colon cancer in women and rectal cancer in men[16]. Also these results are against that of **Freedman, et al., 2009**and also agree with **Arai, 2007**showed that the equal male to female rates of CRC[17, 18].This is contrast may be due to different sample size.

In our study the main presenting symptom in colon cancer is abdominal pain (34%) and bleeding per rectum in cancer rectum (37.8%) while in **Mohamed Said et al., 2013** they found that the main presenting symptom is bleeding per rectum (53.3%)[19].

In our study the colon is more affected than rectum and left side more than the right 68.1% versus 17 % respectively and stage III is the most common stage, while in **(Veruttipong et al., 2012)** study in Gharbiah in Egypt The colon was the commonest site and the right and left sides were equally affected. Stage II disease was the commonest stage[12].While in **Aljebreen, 2007** study in Saudi Arabia The tumor was located in the rectum in 54 patients (48%), in the sigmoid or descending colon in 28%, in the transverse colon in 3.5%, and 22% had right-sided lesions (ascending colon or cecum). Left-sided lesions constituted 76% of all tumors[14].

This difference may be due to lack of public education about signs and symptoms of colon cancer.

As regard survival the median survival in our study was 18.6 months in cancer colon group and 13.2 months in rectal cancer group in **Zeeneldin et al., 2012** the median survival for colon cancer was 18 months versus26 months in rectal cancer group[3].this difference as regard rectal cancer survival may be due to late presentation in rectal cancer group.

In our study there were statistical significance correlation between tumor stage and survival.these results agree with **Jun Li. et al., 2014** which show that T stage affect colorectal cancer survival more significantly than N stage[20].

In our study poor performance status, advanced stage, presence of metastases and elevated CA 19.9 are associated with poor survival in colon cancer group and advanced stage and disease progression at initial response in rectal cancer group.

While in **Zeeneldin et al., 2012** advanced stage, presence of comorbidities and non-use of surgery or chemotherapy were significantly associated with poor median overall survival (OS) and progression free survival (PFS[3]). With multivariate analysis, only advanced stage and presence of comorbidities were independent predictors of poor OS.

Conclusion:

Study of colorectal cancer in Menofia university from 2005 to 2010 revealed that it represents 1.6% of all cancers, colon cancer is more common than rectal cancer, with clear male predominance, it is frequent in patients less than 50 years and urban than rural areas. Patients with colon cancer have better overall survival than rectal cancer. Advanced stage, presence of metastases and elevated CA 19.9 are associated with poor survival in colon cancer group and advanced stage and disease progression at initial response in rectal cancer group.

Recommendations:

We recommend more detailed study based on genetic markers taking in consideration dietary habits and life style variables, especially in young age patients.

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