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COLORECTAL CANCER (CRC);
OBESITY AND ITS CO-RELATION WITH STAGING

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ABSTRACT: Colorectal cancer (CRC) is a common cancer. It has got significant morbidity and mortality. It is a common malignancy. Obesity is defined as BMI equal or above 25.1 kg/m2. Obesity is associated with an increased risk of developing CRC and poor prognosis in patients with colorectal cancer. We conducted a study on 414 patients to look for correlation of obesity with T, N, M and DUKES stage and frequency of obesity in CRC patients. **Period:** It involved all CRC cases presented between 2004 to 2009. **Methods:** It was a single center retrospective chart review. Total patient were 414. Data was collected on Performa and analyzed on SPSS version 19. **Results:** Out of 414 patients males were 243 (58.7%) and females were 171 (41.3%). Mean age was 56 years. It was 57.7 years for males and 54.6 years for females. 221 patients were obese. 123 patients presented in advanced DUKES stage. Mean BMI was 26 and mean CEA level was 76.60. 134 patients presented in advanced T stage (T_3 and T_4). 20% patients with positive polyp history were obese while 80% patients with positive polyp history were non obese. Majority of patients with family history of CRC, previous history of IBD, smoking and previous colonoscopy were non obese. Abdominal pain, abdominal distension, constipation, bleeding per rectum and fever were more common in obese patients but this difference was not statistically significant. About 56% of patients with abdominal pain and abdominal distension were obese and about 59% of patients with constipation and bleeding per-rectum were obese. About 65% of diabetic and hypertensive patients were obese (P value 0.01, 0.01) while 70% patients with coronary artery disease were obese. **Conclusion:** CRC affects more males and advanced age group. Obese CRC patients are more than non-obese patients but obesity is not associated with advanced stage of disease. Co-morbidities like diabetes mellitus, hypertension are more common in obese CRC patients.

Key words: Colorectal Cancer (CRC), Obesity, DUKES Stage, TNM Stage, Body Mass Index

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INTRODUCTION

Colorectal cancer is one of the common malignancies. It has got high morbidity and mortality if not treated in time. CRC represents 15% of all newly diagnosed cancers with annual incidence of 1 million new cases worldwide. It is a common malignancy in both genders, In the USA CRC accounts for approximately 145,000 new cases and 56,000 deaths each year.[1]

CRC epidemiology varies markedly around the world. It is the third most commonly diagnosed cancer in males and second in females globally. Age and male sex are very important risk factors. The incidence of colorectal cancer begins to rise at age 40 and peaks between ages 60 and 75. The incidence increases with age in both males and females and this effect is seen more in left sided cancers.[2] Colon cancer is common after 40 years of age and majority of cases develop after 50 years of age.[3]

Over weight is defined as BMI of 25.1kg/m2 to 27.0kg/m2 and obesity is defined as BMI equal or above 27.1kg/m2. It has been shown that being obese confers an approximately 1.5-fold increased risk of developing CRC relative to being normal weight.[4,5] Increase in BMI is associated with increased incidence of colon and rectal cancer both in men in women. In addition there is increased recurrence reported in literature. Obese patients have poor prognosis and reduced

overall survival.[6,7,8,9]

Higher waist to hip ratio (WHR) is associated with increased risk of colonic polyps in left colon and distal tumor site in young patients.[10,11] Obesity is associated with poor prognosis and significant disease recurrence at local site, but this association was seen only in female CRC patients.[12,13,14,15]

Other studies show that obesity was not predictive of cancer recurrence in women, nor was BMI predictive of overall mortality in men or women[14,15] Moreover, BMI was not associated with survival neither it was an independent prognostic factor of long-term survival in cancer of the colon without metastasis, but it did show that the TNM stage, ASA score, surgical technique, age at surgery, and the immune cell response were prognostic factors.[16]

It was not investigated if obesity is related to advanced disease in CRC patients in Saudi population. That is why we conducted a study on 414 patients to look for correlation of obesity with T, N, M and DUKES stage and frequency of obesity in CRC patients.

MATERIALS AND METHODS AND STATISTICAL ANALYSIS

This was a single centered retrospective chart review. It involved all CRC cases confirmed histopathologically presented to our hospital from 2004-2009. A total of 414 patients were collected. Many of these patients were diagnosed first time in our hospital but a few of them were reviewed. Patients with anal carcinoma or non-adenocarcinoma, like Lymphoma were excluded from our study. The records of all patients were reviewed and medical and demographic information was collected, analyzed and interpreted. The study was done in King Abdul-Aziz medical city (King Khalid National Guards hospital and Princess Noorah Oncology Center, Jeddah, Kingdom of Saudi Arabia).

Data was collected from the electronic media, hospital intranet, electronic laboratory system, and file reviews in medical records. The data was collected and separate Performa was filled on pre approved performa for each patient. The information was gathered in excel files and was converted in SPSS files. All statistical calculation were performed using to SPSS version 20.

RESULTS

Among a total of 414 patients, the male patients were 243 (58.7) % and female patients were 171 (41.3%). Mean age for male patients was 57.7 years (range: 18 to 97 years) and for female patients was 54.6 years (range: 15 to 112 years) (P=0.03). The number and percentage of obese patients was 221 (53.3%) Obese patients presented in DUKES C or D class were 123(55.65). Table-I shows mean, median, Standard deviation, Minimum and maximum values in Age, BMI, tumor length and CEA level. Table-II and III show comparison between obese and non-obese patients in relation with different variables. Table-IV shows Obese and non-obese patients in relation with TNM and DUKES class.

	AGE	BMI	TUMOR LENGTH	CEA LEVEL
Mean	56.36	26.06	5.51	76.60
Median	56.00	26.00	5.00	3.55
Std. Deviation	14.66	5.73	2.65	465.14
Minimum	15	12.46	1	0
Maximum	97	57.69	15	6524

Table-I. Mean, Median, Standard deviation, Minimum and Maximum values

VARIABLES		BMI Groups		TOTAL	P-Value
		Less or equal to 25	Greater than 25		
Family History of CRC	Yes	05	07	12	0.973
	No	156	214	370	
Previous. H/O IBD	Yes	01	02	03	0.753
	No	160	218	378	
H/O Colon Polys	Yes	8	2	10	0.014
	No	153	219	372	
H/O Smoking	Yes	14	10	24	0.097
	No	147	211	358	
Previous Colonoscopy	Yes	3	4	07	0.969
	No	158	217	37	
Loss of Appetite	Yes	54	47	101	0.007
	No	107	174	281	
Abdominal Pain	Yes	86	113	199	0.659
	No	75	108	183	
Abdominal Distension	Yes	32	41	73	0.745
	No	129	180	309	
Diarrhea/Loose Motion	Yes	23	22	45	0.195
	No	138	199	337	
Constipation	Yes	49	71	120	0.725
	No	112	150	262	
Bleeding Per Rectum	Yes	84	122	206	0.557
	No	77	99	176	

Table-II. Comparison between obese and non-obese patients in relation with different variables

VARIABLES		BMI Groups		Total	P-Value
		Less or equal to 25	Greater than 25		
Symptomatic Anemia	Yes	11	09	20	0.236
	No	150	211	361	
Fever	Yes	01	05	06	0.201
	No	160	215	375	
Hemoccult Test	Yes	01	03	04	0.480
	No	160	216	376	
Extra GI Symptoms	Yes	06	09	15	0.857
	No	155	211	366	
Presence of Metastasis	Yes	63	71	134	0.270
	No	97	139	236	
Surgical Intervention	Yes	130	183	313	0.117
	No	31	28	59	
Radiotherapy	Yes	50	60	110	0.897
	No	110	136	246	
Chemotherapy	Yes	136	173	309	0.361
	No	25	41	66	
Diabetes Mellitus	Yes	35	66	101	0.015
	No	126	132	258	
Hypertension	Yes	29	59	88	0.010
	No	132	139	271	
Coronary Artery Disease	Yes	07	17	24	0.110
	No	154	181	335	

Table-III. Comparison between obese and non-obese patients in relation with different variables

		BMI ≤25	BMI > 25	Total	P Value
GENDER	Male	117	126	243	P = 0.52
	Female	76	95	171	
	Total	**193**	**221**	**414**	
M	M0	96	136	232	P = 0.12
	M1	73	73	146	
	Total	**169**	**209**	**378**	
N	0	46	76	122	P = 0.07
	1	60	55	115	
	2	31	28	59	
	3	1	1	2	
	Total	**138**	**160**	**298**	
T	1	2	4	6	P = 0.25
	2	13	21	34	
	3	99	115	214	
	4	27	19	46	
	Total	**141**	**159**	**300**	
DUKES	A	4	6	10	P = 0.13
	B	40	73	113	
	C	54	56	110	
	D	63	67	130	
	Total	**161**	**202**	**363**	

Table-IV. Obese and non-obese patients in relation with TNM and DUKES class

DISCUSSION

Multiple studies have shown that obesity is associated with increased risk of developing CRC, however the influence of obesity on the stage of CRC is not investigated and is not studied in our part of world. Our study is first of its kind in this regard.

The latest Saudi Cancer Registry and Cancer Incidence Report Saudi Arabia published in 2014 showed more male patients affected (52.9%) than female patients (47.1%). CRC was ranked first among males and third among females. The percentage of male and female was 58% and 42% respectively in Saudi Cancer registry and similarly in our study male and female were also 58% and 42% respectively.

Maximum patients were diagnosed in 2009. Maximum obese patients were in 2006 (74.6%). 20% patients with positive polyp history were obese while 80% patients having positive polyps history were non obese. 41% patients with negative polyps history were non obese and 59% patients were obese.

When different variables were compared with BMI, surprisingly more patients with previous history of colonic Polyps had normal BMI (P-value 0.01). Majority of patients with family history of CRC, previous history of IBD, smoking and previous colonoscopy were non obese (P-value 0.97, 0.75, 0.10 and 0.07 respectively).

When we look at symptoms, majority of patients with anorexia, abdominal pain, alternative bowel habits were not obese (P-value 0.01, 0.66 and 0.20). Majority of patients with constipation, fever, positive occult blood in stool, patients with metastasis, diabetic patients, hypertensive and patients with ischemic heart disease were obese. (P-values 0.73, 0.20, 0.48 and 0.27 respectively)

More obese patients received chemotherapy and radiotherapy than non-obese patients but this difference was not significant (P-value > 0.05).

Renehan AG and colleagues[6] noted positive association between obesity and CRC. This association was stronger in males than females. Giovannucci and colleagues[5] noticed inverse relationship between physical activity and risk of colon cancer. They also noticed direct association between obesity and CRC.

Sinicrope FA[9] and colleagues noted that 20% of all CRC patients were obese and these patients had more distal tumors while in our study 122/221(55%) obese patients had distal tumors. Thompson and colleagues[10] confirmed strong association between waist to Hip ratio (WHR) and development of colon neoplasia and colonic polyps.

Asgari Jaffar Abadi[12] observed strong association between CRC and obesity. In the study of sinicrope[11] 23% patients were obese while 221/414 (53.3%) patients were obese in our study. They also noticed association of obesity with distal tumor site. In our study 122/221(55%) patients with distal tumors were obese.

CONCLUSION

CRC affects old age group and is more common in male patients. About half of CRC patients were obese in our study. Constipation, abdominal pain and bleeding per rectum were most common symptoms among obese patients. About half of obese patients present in advance TNM and DUKES stage. Co-morbidities like diabetes mellitus, hypertension are more common in obese CRC patients.

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"You can't build a reputation on what you're going to do."

Henry Ford

AUTHORSHIP AND CONTRIBUTION DECLARATION

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