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Changing Patterns of Colorectal Cancer in Hail Region

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***Abstract*—**Background and Objectives: Colorectal carcinoma is increasing among both men and women worldwide. It has a multifactorial etiology including genetic factors, environmental factors and inflammatory conditions of the digestive tract. A clinicopathologic assessment of colorectal carcinoma in Hail region is done, considering any changing patterns in two 5-year periods from 2005-2009 (A) and from 2012 to 2017 (B). All data had been retrieved from histopathology files of King Khalid Hospital, Hail. Results: During period (A), 75 cases were diagnosed as colorectal carcinoma. Male patients comprised 56/75 (74.7%) of the study, with a mean age of 58.4 (36-97), while females were 19/75 (25.3%) with a mean age of 50.3(30-85) and the difference was significant ($p = 0.05$). M:F ratio was 2.9:1. Most common histological type was adenocarcioma in 68/75 (90.7%) patients mostly well differentiated in 44/68 (64.7%). Mucinous neoplasms comprised only 7/75 (9.3%) of cases and tended to have a higher stage ($p = 0.04$). During period (B), 115 cases were diagnosed with an increase of 53.3% in number of cases than period (A). Male to female ratio also decreased to 1.35:1, females being 44.83% more affected. Adenocarcinoma remained the prevalent type (93.9%), while mucinous type was still rare (5.2%). No distal metastases found at time of presentation. Localization of tumors was rectosigmoid in group (A) in 41.4%, which increased to 56.6% in group (B), with an increase of 15.2%. Iliocecal location also decreased from 8% to 3.5%, being 56.25% less. Other proximal areas of the colon were decreased by 25.75%, from 53.9% in group (A) to 40% in group (B). Conclusion: Colorectal carcinoma in Hail region has increased by 53.3% in the past 5 years, with more females being diagnosed. Localization has also shifted distally by 15.2%. These findings are different from Western world patterns which experienced a decrease in incidence and proximal shift of the colon cancer localization. This might be due to better diagnostic tools, population awareness of the disease, as well as changing of life style and/or food habits in the region.

***Keywords*—**Colorectal cancer, Hail Region, changing pattern, distal shift.

I. Introduction

COLON cancer is a multifactorial carcinoma including several etiological factors such as environmental exposures, genetic factors, and inflammatory conditions of digestive tract as well as diet. It is still one of the most common cancer-related morbidity and mortality in the whole world. Although its incidence is decreasing in some parts of the worlds, other areas experience an increase due to changing life style and adopting different dietary habits [1].

Currently, surgery is the definitive treatment modality for colonic adenocarcinoma mainly hemi colectomy. Recent advances in endoscopy for digestive tract have largely contributed to early detection of premalignant and early cancerous lesions [2].

A change in the anatomic distribution of colorectal carcinoma has been reported by recent epidemiological studies in Western world, mainly undergoing a shift from distal to proximal site. It has been reported that cecal and ascending colon tumors as well as tumors of transverse colon have increased from 33.9% to 36% and from 15.8% to 17.2% respectively. On the other hand, tumors of sigmoid colon decreased from 36% to 33.4%. However other studies in other parts of the world reported no evidence for a proximal shift of colon cancer [3].

In the present study we aimed at studying colorectal carcinoma cases over a 2-period time, from 2005-2009 and from 2012-2017, to determine if there was any changing pattern or site (proximal or distal) shift, comparable to other parts of the world during the past 10 years in the region of Hail, KSA.

II. Material and Methods

Cases of colorectal carcinoma had been retrieved from histopathology files of King Khalid Hospital, Hail, during the years 2005-2009 (Period A) and from 2012-2017 (Period B). Clinicopathological data for each patient were recorded whenever available. For each patient age, gender, localization of tumor, and histological diagnosis was recorded. Localization was divided according Li and Lai [4], into right-sided tumors proximal to the splenic flexure (cecum, ascending colon and transverse colon), left-sided tumors arising distal to this site (descending colon, sigmoid colon), and rectal tumors. Histopathological classification and grading has been done according to a modification of the WHO/UICC classification [5].

Percentage of change was calculated as: (V2-V1) /V1X100, where V1=1st value, V2 = 2nd value.

An SPSS 19 statistical program was used to calculate p-value, which was considered significant if < 0.05.

III. Results

Total number of cases diagnosed in the two periods of study was 190 colorectal carcinomas. During period A (2005-2009), 75 cases of colorectal carcinoma were diagnosed, while 115 cases were diagnosed during period B (2012-2017). The

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percentage of increase in total number of cases was 53.3% (Fig. 1). Carcino-embryonic antigen (CEA) results were available for 12 cases Table I.

TABLE I
CHARACTERISTICS OF PATIENTS WITH DOCUMENTED CEA RESULTS

No.	age	gender	Presenting symptom	Type of tumor	Grade	CEA	CA19.9
1	54	F	Rectal mass with partial intestinal obstruction	Adenocarcinoma	Grade II	19.85	Not available (NA)
2	68	M	Rectal mass	Adenocarcinoma	Grade II	0.8	NA
3	57	M	Rectal polyp and mass	Adenocarcinoma	Grade I	0.98	NA
4	81	M	Rectal mass, constipation, bleeding per rectum	Adenocarcinoma	Grade II	147	121.4
5	43	F	Bleeding per rectum	Adenocarcinoma	Grade II	104.9	NA
6	35	F	Rectal mass 5 cm from anal verge with bleeding, weight loss	Adenocarcinoma	Grade I with high grade dysplasia	Normal	NA
7	47	M	Colonic mass with ascites	Adenocarcinoma	Grade III	Normal	321
8	49	M	Intestinal obstruction Sigmoid ulcerated mass	Adenocarcinoma	Grade I	7.98	118.7
9	43	F	Bleeding per rectum, Polypoid mass	Adenocarcinoma	Grade I	75.7	40.2
10	60	F	Sigmoid Mass	Adenocarcinoma	Grade I	Normal	2.01
11	73	M	Rectal Mass	Mucinous Adenocarcinoma	Grade III	501	NA
12	47	F	Rectal Mass	Adenocarcinoma	Grade I	Normal	Normal

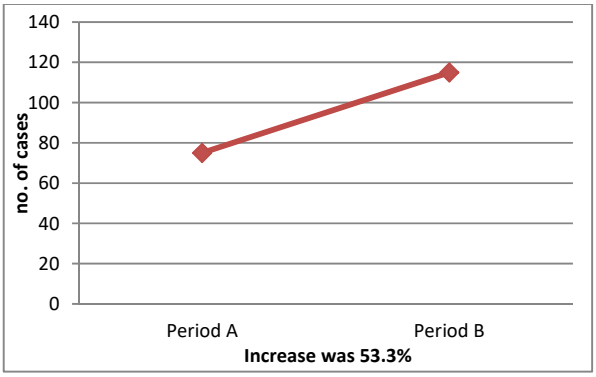

Fig. 1 No of Cases Studied between 2005-2009 (A) & 2012-2017 (B)

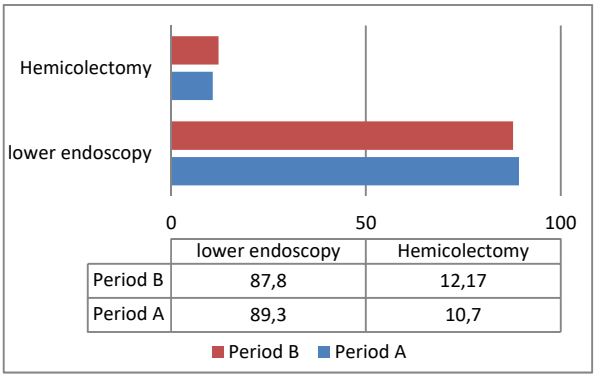

Fig. 2 Diagnostic Methods for Cases Studied

Colorectal carcinomas in our series presented as a mass in 43.6% of cases, showing either a large hard necrotic fungating mass, ulcerated, or polypoid mass. In 29.1% the presenting symptom was bleeding per rectum, while in 26.43% of cases, intestinal obstruction was the presenting symptom. One case (0.87%) presented as metastases. One case had a positive family history of colon cancer and another case had a history of polyposis syndrome.

The vast majority of cases (89.3% & 87.8%) were diagnosed by lower endoscopy and the remaining was diagnosed by hemi colectomy (Fig. 2).

As regards numbers and male to female ratio, the rate of change was a decrease in males, 23.16%, and an increase in females, 17.3% (Fig. 3, Table II).

Mean age for males was 58.4 years and 53.13 years and for females 50.3 and 53.04 years in groups A & B respectively (Table I). The age group mostly affected for both males and females was 40-69 years of age. (Fig. 4, Table II).

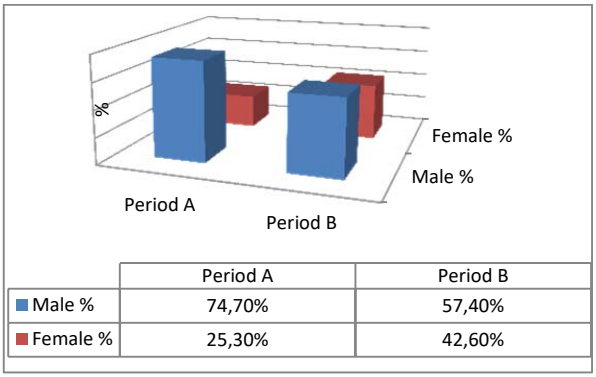

Fig. 3 Male and Female % Distribution in Time Periods Studied

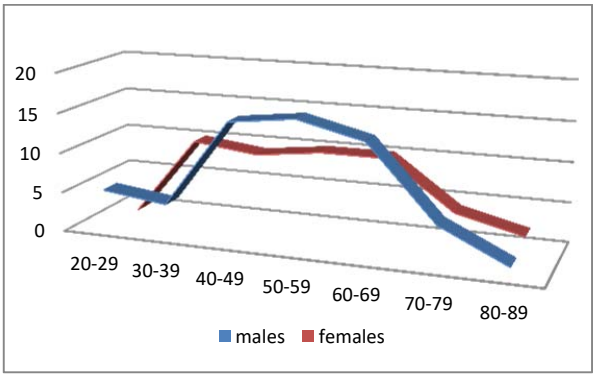

Fig. 4 Age Groups in Colorectal Carcinoma Studied

Most of our carcinomas in both periods of time were

adenocarcinomas (Table III). Histopathological reviewing of the specimens had been done and revealed well differentiated tumors in 64.7% and 34.25% of periods A and B respectively (rate of decrease was 47.1%). Simple or complex tubules with well polarized nuclei, uniform in size, and close in resemblance to precursor lesions were seen in grade I tumors (Figs. 5 (A) & (B)). Moderately differentiated adenocarcinomas (Figs. 5 (C) and (D) were diagnosed in 25% and 63.9% respectively. Rate of increase was 155.6%, while poorly differentiated tumors were diagnosed in 1.85% of cases in the period between 2012 and 2017. Mucinous neoplasms were seen in 10% and reduced to 5.2% in 2012-2017 (48% rate of decrease). A single squamous cell carcinoma had been diagnosed during the whole period of study (Table III).

TABLE II
GENDER AND AGE DISTRIBUTION IN 2 PERIODS STUDIED

	Male no. (%)	Female no. (%)	Male mean age (Range)	female mean age (Range)	M:F Ratio
Period A	56/75 (74.7%)	19/75 (25.3%)	58.4 (36-97)	50.3 (30-85)	2.9:1
Period B	66/115 (57.4%)	49/115 (42.6%)	53.13 (20-78)	53.04 (32-85)	1.35:1

TABLE III
HISTOLOGICAL SUBTYPES OF COLONIC CARCINOMA STUDIED

Type of Tumor	Period A	Period B	Percentage of Change
Adenocarcinoma: Total No.(%)	68/75 (90.7%)	108/115 (93.9%)	Increased by 4%
Well Differentiated (grade 1)	44/68 (64.7%)	37/108 (34.25%)	Decreased by 47.1%
Moderately Differentiated (grade II)	17/68 (25%)	69/108 (63.9%)	Increased by 155.6%
Poorly Differentiated (grade III)	0/68 (0%)	2/108(1.85%)	
Mucinous Carcinoma	7/68 (10.3%)	6/115 (5.2%)	Decreased by 49.5%
Squamous Cell Carcinoma	0%	1/115 (0.9%)	

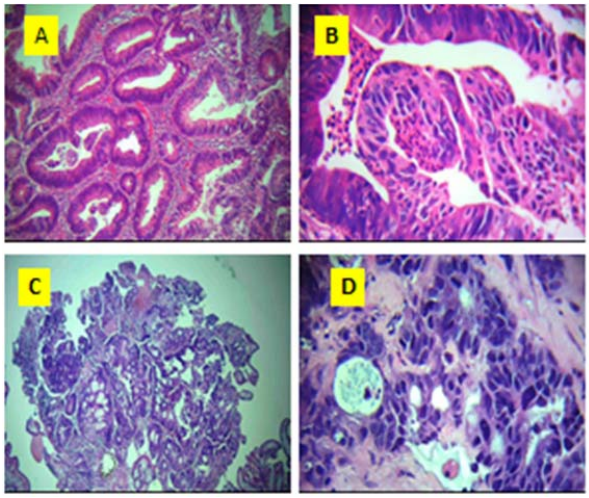

Fig. 5 (A) Well differentiated colonic adenocarcinoma with well-formed glandular structures H&E X100; (B) A higher power showing disorientation of lining cells, together with an intraepithelial neutrophilic infiltrate H&E X 400; (C) A moderately differentiated adenocarcinoma of the colon showing fused glands in an adenoid cystic pattern. H&E X 40; (D) A higher power view showing cystic glands lined by enlarged pleomorphic malignant cells with loss of polarity. H&E X 400

Localization of colonic carcinoma during time period from 2015-2009 was 56% proximal to the splenic flexure including cecum, ascending colon, hepatic flexure and transverse colon. The percentage of cases has decreased to 41% (the decrease was 26.8%). Distally located neoplasms (splenic flexure, descending colon, sigmoid colon and rectum) were 41.3%, and increased to 59% during 2012-2019. The rate of increase was 42.9% (Table IV).

As regards age groups affected according to localization, the most affected age group affected by colonic carcinoma for both males and females was 60-69 years (Fig. 6). As regards rectal tumors, the most affected age group was 50-59 for females and 60-69 for males (Fig. 7).

TABLE IV
LOCALIZATION OF COLONIC CARCINOMA IN BOTH STUDIED PERIODS

Localization	2005-2009 (Period A)	2012-2017 (Period B)	% of change
Proximal colon	48%	37%	Decreased by 22.9%
Cecum	8%	4%	Decreased by 50%
Recto-sigmoid	**41.3%**	**59%**	**Increased by 42.86%**
Metastatic	2.7%	0%	

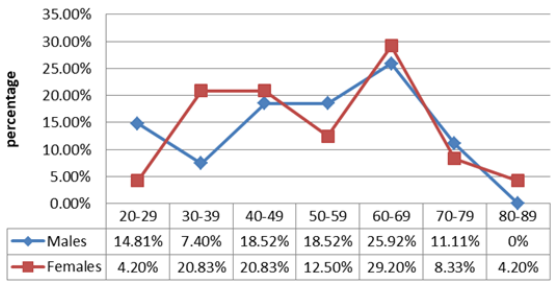

Fig. 6 Colonic Localization in relation to Age groups

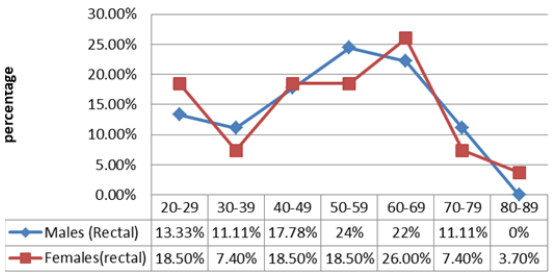

Fig. 7 Rectal Localization in relation to Age groups

IV. Discussion

Anatomic, embryologic and metastatic patterns are the main differences among colon and rectal carcinomas [1]-[3]. Different genetic abnormalities found in colorectal cancers differ according to site, proximal colon cancer being related to the nucleotide instability pathway, as microsatellite instability (MSI), while distal colon cancer is associated with chromosomal instability (CIN) [4]. Different drug targets are also considered such as v-raf murine sarcoma viral oncogene homolog B (BRAF), which is mutated in proximal colon cancers, and the epidermal growth factor receptor (EGFR), which is mostly amplified or overexpressed in distal colorectal cancers [5], [6].

Several studies have dealt with the change of pattern of colorectal carcinomas over the past 10 years. Western studies have pointed to a "proximal shift" of colon carcinoma in several studies, sometimes linking the change to dietary factors [7]-[11]. However, studies from other parts of the world failed to confirm such trend. Park et al. reported an increase in both proximal and distal compartments of the colon [6], while other studies confirmed a proximal shift [12], [13].

In the present study, total number of colorectal carcinomas increased in incidence by 49.8% from the period 2005-2009 (A) towards 2012-2017 (B). There was also a distal shift towards distal colon and rectum rather than a proximal one. This shift was found in both males and females, and was not related to a certain age group. Most of the carcinomas studied were detected in either sigmoid colon or rectum, distal to splenic flexure. This distal shift having increased by 42.86%, while, at the same time, proximal colon tumors decreased by 22.9% (Table IV). This finding was only supported by a study from Iran in 2012, where proximal shift reported by Western countries could not be validated [10].

In an experimental study, a correlation between diet in colorectal carcinoma and distal shift had been postulated. Animals fed by high fat/high caloric diet showed a change from right to left side colonic carcinomas [14].

In a recent study in Hail region, colorectal carcinoma was counted as the most prevalent cancer in males and the 3rd most common cancer in females, preceded by breast and thyroid carcinoma [15]. Increased numbers of females was noted during the last period from 2012-2017 in Hail regions, where male to female ratio decreased from 2.9:1 in period A to become 1.35:1 in period B (Table II). However, increasing incidence in both males and females has been documented in other parts of Saudi Arabia [16]-[19].

The increase in risk for colorectal carcinoma had been linked to a diet rich in animal proteins, fat and poor in vegetables and fruits, together with physical inactivity as well as increased body mass index. Genetic predisposition, positive family, adenomatous polyps and inflammatory bowel disease including Crohn's disease and ulcerative colitis are considered as risk factors [20]-[24]. However in the present study, one case had a family history of colonic carcinoma and another had a polyposis syndrome.

In the present study, age groups mostly affected in both males and females were from 40-49, 50-59, and 60-69 (Fig. 4). A peak at the age group 60-69 could be found denoting older people being affected by distal colon and rectal carcinomas (Figs. 6 & 7). This was in accordance with other regions in Saudi Arabia [16]. However, a study done in Alexandria, Egypt reported more than 25% of colorectal carcinomas are less than 40 years [25]. An age-dependent shift had been recorded by several international studies [26]-[29], which could not be observed in our study.

As regards histopathological type, adenocarcinomas were prevalent in our study with few mucinous tumors. This was in accordance with other studies worldwide [30]-[32]. However, more moderately-differentiated tumors are recorded recently, with decrease in metastatic presentation.

To conclude, according to our study, colorectal carcinoma is prevalent and increasing in incidence in Hail region, especially in the past 5 years, with more females being affected. A distal rather a proximal shift is noted with more carcinomas arising in distal colon and rectum in both males and females. Further epidemiological studies are recommended to find the effect of changes in diet, if any that is affecting the distal shift. Moreover, molecular genetic studies are encouraged to detect microsatellite instabilities or chromosomal abnormalities on a larger group study.

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