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# Histopathological pattern of colorectal cancer in relation to age and gender in northern saudi arabia

## Abstract

**Background:** Colorectal cancer (CRC) is one of the leading causes of cancer-related deaths worldwide. There are different histopathological variants of CRC that differ in behavior and means of management. Therefore, the aim of this study was to determine the different types CRC in relation to age and gender in Northern KSA.

**Methodology**: A retrospective cohort study was carried out over a five year period in different referral hospitals. In this study 120 files were retrieved from departments of Surgery from different hospitals in Northern KSA.

**Results**: Most patients presented with colonic site tumors constituting 67/120(55.8%), followed by Recto-sigmoid, and Rectum representing 31/120(25.8%) and 13/120(10.8%) respectively. Adenocarcinoma (AD) was diagnosed in 105/120(87.5%).The great majority of patients were categorized with moderately differentiated carcinoma representing 76/120(63.3%), followed by well differentiated and poorly differentiated carcinomas constituting 35/120(29.2%) and 9/120(7.5%), respectively.

**Conclusion:** Saudi patients with CRC were more expected to present with more advanced stages of the disease and at younger ages compared to Western populations, which presents more frequently in an extra advanced stage and poorly differentiated type than in older patients.+

**Keywords:** colorectal cancer, saudi arabia, adenocarcinoma, colon

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## Introduction

Colorectal cancer (CRC) is one of the highly frequent cancers worldwide.[1] CRC is the 3rd most common cancer in men and the second most common cancer in women.[2] CRC is a multifactorial disease linked to lifestyle, genetic and environmental factors. Although, there are hereditary and non-hereditary CRC types, but the majority is non-hereditary and commonly caused by somatic mutations in response to environmental factors. In the past fewyears, scientists have concentrated their thoughtfulness on the mechanisms behind these factors and the methods of enhancing disease prevention and treatment.[3]. CRC is not a homogenous disease, but can be classified into different subtypes, which are characterized by specific molecular and morphological alterations.[4] Although outcomes of CRC have improved, it is clear that from a genomic standpoint CRC is not one disease, but a heterogeneous group of malignancies that arise within one organ. This means that different subtypes have different outcomes; the ability to subtype tumors in the clinic would be highly favorable, enabling optimal treatment for individual patients.[5]

The most common (about □84 % of sporadic CRC) is characterized by chromosomal instability (CIN), with gross changes in chromosome number and structure. These are often detectable as a high frequency of DNA somatic copy number alterations (SCNA), which are a hallmark of most tumors that arise by the adenoma-carcinoma sequence.[4] Previous molecular genetic studies have associated CIN with inactivating mutations or losses in the Adenomatous Polyposis Coli (*APC)* tumor suppressor gene, which occurs as an early event in the development of neoplasia of the CRC in this sequence. The second group (around 13-16 % of sporadic CRC) are hyper-mutated and show microsatellite instability (MSI) due to defective DNA mismatch repair (MMR), often associated with wild-type *TP53* and a near-diploid pattern of chromosomal instability.[6,7]

With regard to epidemiology of CRC, countries with the highest incidence rates include Australia, New Zealand, Canada, the United States, and parts of Europe. The countries with the lowest risk include China, India, and parts of Africa and South America.[8,9] CRC has been the most common cancer among men and the third commonest among women since 2002 in KSA. There has been a slight predominance among men with an average ratio of 116:100 over theyears (range: 99:100-132:100). The overall age-standardized rate (ASR) approached a plateau of 9.6/100000 in 2010. The incidence of the disease has been highest in the capital, Riyadh, where it reached 14.5/100000 in 2010. Data on CRC for the period 1994-2010 was extracted from the Saudi Cancer Registry. The King Faisal Specialist Hospital and Research Center (KFSHRC) Cancer Registry showed that CRC presents at a younger age in Saudis, especially in women. This has a major implication for decisions about the threshold age for screening.[10] Therefore, the aim of this study was to determine the different types CRC in relation to age and gender in Northern KSA.

## Materials and methods

This is a descriptive retrospective study conducted in Northern KSA. Sample size represents a full coverage of the available cases with completed required data (including full histopathology report, age, sex etc.). Any patient underwent colonoscopy or/and biopsy due to the presence of colon lesion for the purpose of diagnosis was included. Of the 353 retrieved files, 120 were found to be referring to colonoscopy or/and biopsy. All information of the patients was retrieved from the concerned hospitals. All 120 patients were confirmed by conventional histopathology. Conventional histopathology was re-assessed. The histological examination of biopsy specimens were done to achieve the assessment process role, by giving a pathology category classification (types of malignant lesions).

## Statistical analyses

Data managing was completed by using the Statistical Package for Social Sciences (SPSS version 16; SPSS Inc, Chicago, IL). SPSS was used for analysis and to do Fisher exact test for statistical significance (P value < 0.05 was considered significant). The 95% confidence level and confidence intervals were applied.

# Results

This study investigated 120 CRC patients their ages ranging from 20 to 90years with a mean age of 63years old. Out of the 120 patients 64/120(53.3%) were males and 56/120(46.7%) were females giving males' females' ratio of 1.14: 1.00. Most of the study population were found in age range 61-70 representing 33/120(27.7%) followed by age ranges 71-80, 51-60, 41-50&81+ and <40years constituting 20/120(16.7%), 19/120(15.8%), 17/120(14.1%)&17/120(14.1%) and 14/120(11.8%), respectively as indicated in Table 1 & Figure 1. The number of patients presented at relatively younger age was 30/120(25%). The distribution of males and females in each age group was relatively varied. High variations were encountered in age group <40years and 61-70years. In age range < 40years, the proportions of males and females were 28.6% and 71.4% in this order. In age group 61-70, the proportions of males and females were 70% and 30% in this order. The remaining age groups, however, showed relatively similar proportions, as shown in Figure 1.

**Table 1** Distribution of the study subjects by sex and age

| Age group | Males | Females | Total |
|---|---|---|---|
| <40 years | 4 | 10 | 14 |
| 41-50 | 9 | 8 | 17 |
| 51-60 | 8 | 11 | 19 |
| 61-70 | 23 | 10 | 33 |
| 71-80 | 11 | 9 | 20 |
| 81+ | 9 | 8 | 17 |
| Total | 64 | 56 | 120 |

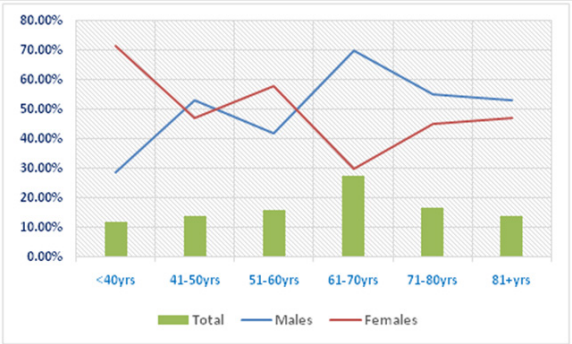


**Figure 1** Description of the study subjects by age and sex.

With regard to the site of the tumor, most of them were upraised in the colon constituting 67/120(55.8%), followed by Recto-sigmoid, and Rectum representing 31/120(25.8%) and 13/120(10.8%) respectively, as indicated in Table 2. Out of the 67/120(55.8%) presented with colonic lesions, 35/67 (52%) were females and 32/67(48%) were males. Of the 31/120(25.8%) identified with recto-sigmoid tumors, 18/31(58%) were males and 13/31(42%) were females, as indicated in Table2 Figure 2.

In the assessment of tumor differentiation, the great majority of patients were categorized with moderately differentiated carcinoma representing 76/120(63.3%), followed by well differentiated and poorly differentiated carcinomas constituting 35/120(29.2%) and 9/120(7.5%), respectively. The risk associated with patients to present with relatively advanced stages of the CRC was found to be statistically significant P < 0.0001. Out of the 76 patients with moderately differentiated carcinomas, 39/76(51.3%) were males and 37/76(48.7%) were females. Out of the 35 patients with well differentiated 21/35(60%) were males and 14/35(40%) were females, as shown in Table2 & Figure 4. Moreover males were more frequent to present with early stages of the disease than females and this was found to be statistically significant P < 0.05.

**Table 2** Distribution of the study subjects by sex and pathology

| Category | Variable | Males | Females | Total |
|---|---|---|---|---|
| **Tumor presentation** | | | | |
| | Colon | 32 | 35 | 67 |
| | Recto-sigmoid | 18 | 13 | 31 |
| | Rectum | 10 | 3 | 13 |
| | Rectal transverse | 4 | 4 | 8 |
| | Rectal polyp | 0 | 1 | 1 |
| | Total | 64 | 56 | 120 |
| **Diagnosis** | | | | |
| | Adenocarcinoma (AD) | 58 | 47 | 105 |
| | Papillary AD | 4 | 3 | 7 |
| | Spindle cell sarcoma | 1 | 0 | 1 |
| | Intra-mucosal AD | 1 | 2 | 3 |
| | AD signet ring type | 0 | 2 | 2 |
| | Squamous cell Carcinoma | 0 | 2 | 2 |
| | Total | 64 | 56 | 120 |
| **Tumor Differentiation** | | | | |
| | Well differentiated | 21 | 14 | 35 |
| | Moderately differentiated | 39 | 37 | 76 |
| | Poorly differentiated | 4 | 5 | 9 |
| | Total | 64 | 56 | 120 |

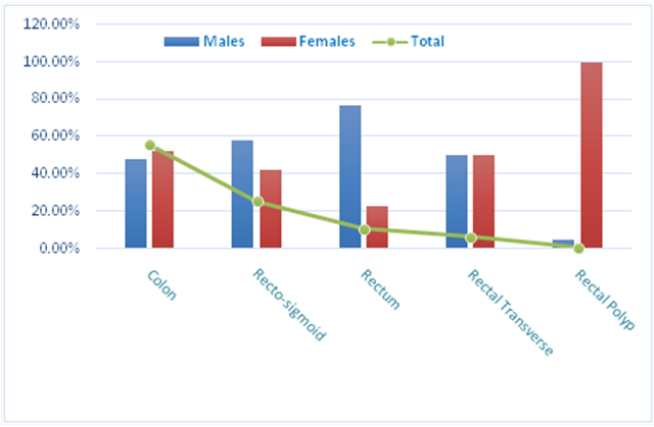


**Figure 2** Description of the study subjects by sex and Tumor site.

Table 3 summarizes the distribution of the study subjects by age and pathology. The majority of the patients with colonic site tumors were identified among age group 61-70years constituting 21/67(31.3%), followed by age ranges 51-60, 41-50, <40 and 81+ representing 13/67(19.4%), 11/67(61.4%), 9/67(13.4%) and 7/67(10.4%), respectively. Most of the cases of recto-sigmoid site were also found in age group 61-70years, representing 7/31(22.6%) followed by 71-80 & <40years and 41-50years representing 6/31(19.4%)&6/31(19.4%) and 5/31(16%) respectively. Out of the 13 cases of rectum site,

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3/13(%) were found in age group 41-50, as well as, in 61-70years, as indicated in Table 3 & Figure 5.

**Table 3** Distribution of the study subjects by Age and pathology

| Category | Variable | <40yrs | 41-50 | 51-60 | 61-70 | 71-80 | 81+ | Total |
|---|---|---|---|---|---|---|---|---|
| **Tumor presentation** | | | | | | | | |
| | Colon | 6 | 9 | 13 | 21 | 11 | 7 | 67 |
| | Recto-sigmoid | 6 | 5 | 2 | 7 | 6 | 5 | 31 |
| | Rectum | 1 | 3 | 2 | 2 | 2 | 3 | 13 |
| | Rectal transverse | 0 | 0 | 2 | 3 | 1 | 2 | 8 |
| | Rectal polyp | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| | Total | 14 | 17 | 19 | 33 | 20 | 17 | 120 |
| **Diagnosis** | | | | | | | | |
| | Adenocarcinoma (AD) | 8 | 15 | 18 | 31 | 17 | 16 | 105 |
| | Papillary AD | 1 | 2 | 0 | 2 | 2 | 0 | 7 |
| | Spindle cell sarcoma | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | Intra-mucosal AD | 2 | 0 | 0 | 0 | 1 | 0 | 3 |
| | AD signet ring type | 1 | 0 | 1 | 0 | 0 | 0 | 2 |
| | SCC | 2 | 0 | 0 | 0 | 0 | 0 | 2 |
| | Total | 14 | 17 | 19 | 33 | 20 | 17 | 120 |
| **Tumor Differentiation** | | | | | | | | |
| | Well differentiated | 4 | 1 | 5 | 12 | 7 | 6 | 35 |
| | Moderately differentiated | 8 | 13 | 13 | 20 | 13 | 9 | 76 |
| | Poorly differentiated | 2 | 3 | 1 | 1 | 0 | 2 | 9 |
| | Total | 14 | 17 | 19 | 33 | 20 | 17 | 120 |

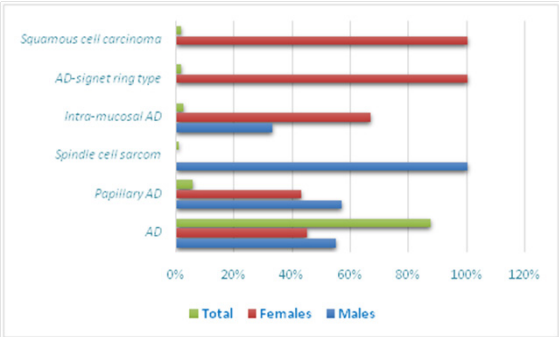


**Figure 3** Description of the study subjects by Sex and Diagnosis.

Out of the 76 patients diagnosed with moderately differentiated carcinoma, 20/76(30%) were identified among age group 61-70years, 13/76(17%) were identified among age ranges, 41-50 & 51-60 & 71-80years, for each. Most of the cases of well differentiated carcinoma were found among age group 61-70years, followed by 71-80, 81+, and 51-60years constituting 12/35(34.3%), 7/35(20%), 6/35(17%) and 5/35(14.3%), in this order, as shown in Table 3 & Figure 7.

## Discussion

In the present study we have assessed the different patterns of CRC in northern Saudi Arabia, as well as, the relation between these CRC types and demographical characteristics, particularly gender and sex. In this study, patients present with different colorectal sites. The great majority presented with colonic site lesions followed recto-sigmoid sites. Right colon tumors spread to local and distant sites in 90% of autopsies, and to distant sites alone in 10%. Rectal tumors spread locally only in 25% of cases, to distant site alone in 25%, and to both in 50%. Regardless of the origin of the primary tumor, the liver is the most common site of metastasis, followed by the regional lymph nodes and the lungs. Two-thirds of the patients with right colon lesions died of liver metastases, and three-quarters of those with rectal tumors succumbed to disseminated disease.[11]

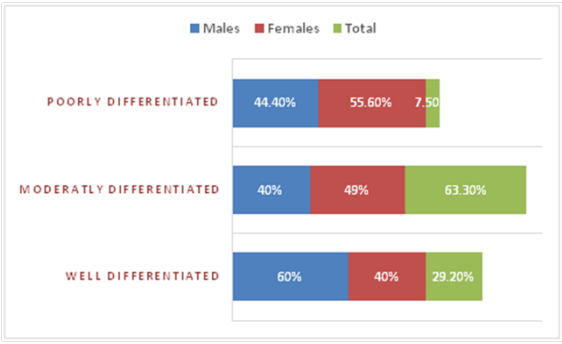


**Figure 4** Description of the study subjects by Sex and Grade of differentiation.

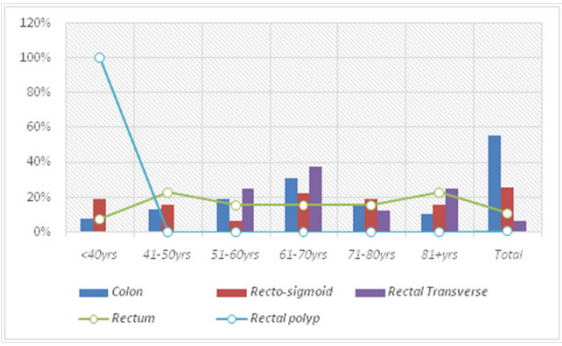


**Figure 5** Description of the study subjects by age and tumor site.

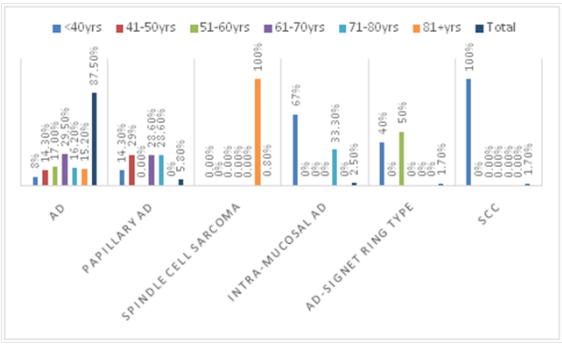


**Figure 6** Description of the study subjects by age and Diagnosis.

Most of patients in this series were diagnosed with adenocarcinoma followed by papillary adenocarcinoma. Colon adenocarcinoma is the most common histopathological type of colorectal cancer. Most patients have mucinous adenocarcinoma, present late, and have rapid disease progression and poor outcome.[12,13]

AD may be well-differentiated, frequently rising within a villous adenoma, or poorly-differentiated. The poorly-differentiated lumps (such as, AD-signet ring type) have a poor prognosis and tend to

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affect younger patients. Most are well-differentiated AD and are classified according to mucin content. Mucin-secreting ADs have less than 50% mucin production, mucinous carcinomas have more than 50% extracellular mucin, and AD-signet ring types have intracellular mucin that shifts the nucleus to one side.[14] Diagnosis of AD-signet ring types is made when at least 50% of the cells are of the signet ring type.[15]

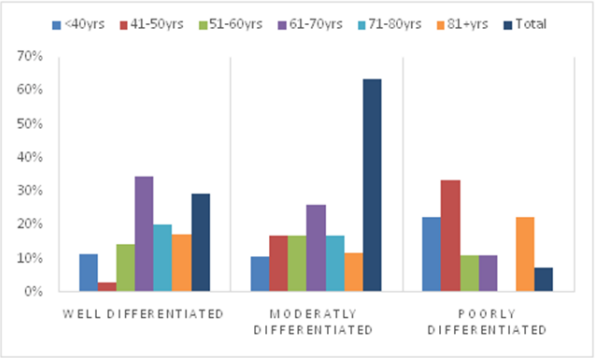


**Figure 7** Description of the study subjects by age and grade of differentiation.

Although the age of patients is relatively similar in all age groups, but it was observed that there was an increase in the younger age group. Moreover, though the males were more than females, but many females present at younger age. Such findings were previously reported from Saudi Arabia. Colorectal cancer has been the most common cancer among men and the third commonest among women since 2002 in KSA. There has been a slight predominance among men with an average ratio of 116:100 over theyears (range: 99:100-132:100). The overall age-standardized rate (ASR) approached a plateau of 9.6/100000 in 2010. Colorectal cancer presents at a younger age in Saudis, especially in women. This has a major implication for decisions about the threshold age for screening. The ASR has increased, but is still much lower than in developed countries.[10,16] In the present study the mean age was 63 and the great majority of the males were found in age range 61-70years, followed by 81+ & 41-50, hence the great majority of females were observed at age range 51-60 followed by 61-70 & <40years.

With regard to the lesion site, females were more frequently seen with colonic site; hence males were more frequent observed with recto-sigmoid site. Rectum site presentation was more common among men compared to females.

The diagnosis of different carcinomas was relatively similar among both sex with exception of squamous cell carcinoma and AD signet ring type were more common among females.

Tumor differentiations were relatively similar for both sex, but what is excitingly, that most cases present in advanced stage of the disease, which might be due to the lack of screening programs as well as, the low levels of awareness. Such findings were reported from different regions in Saudi Arabia. Emergency CRC presentation is common in the Tabuk region. Patients tend to present at an advanced stage, which necessitates an endeavor to detect the disease in its early stages, possibly through initiation of health education programs and suitable screening projects.[17] Another study has reported that CRC in KSA is frequently diagnosed at advanced stages with metastases and is accompanying with poor prognosis and short survival. Nationwide awareness campaigns and screening programs for CRC are critical for prevention, early detection and adequate management of CRC.[18,19]

On the other hand, the age distribution by site of the lesion has showed great variation. Most of those with colonic sites were diagnosed at age range 61-70 followed by 51-60years, hence, most of the those with recto-sigmoid lesion site were diagnosed at the age range 61-70 followed by 71-80 & <40years. Nevertheless, most of the cases of AD diagnosed at age over 61years. Though all cases of papillary adenocarcinoma were diagnosed at age over 61, we noticed that most cases of Intra-mucosal AD and SCC were diagnosed at age less than 40years. It was reported that there is a considerable proximal change of the colorectal carcinoma with more advanced lesions at the time of presentation in Saudi Arabia.[20,21]

For tumor differentiation most cases of the poorly differentiated presented at younger stages of the disease which might be attributed to non-expectation of the disease.

## Conclusion

Saudi patients with CRC were more expected to present with more advanced stages of the disease and at younger ages compared to Western populations, which presents more frequently in a extra advanced stage and poorly differentiated type than in older patients. Such findings necessitate the need for a comprehensive awareness program accompanied by screening program to control this preventable cancer in Saudi Arabia.

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## Conflicts of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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