White Blood Cell Count in Colorectal Cancer Patients, a retrospective study in KHMC

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ABSTRACT

Objectives: To assess white blood cell count (WBC) in colorectal cancer (CRC) patients in King Hussein Medical Center and determine if there is an association between high WBC count as an inflammatory marker and CRC and to find any difference in the pattern of the disease in CRC patients who have leukocytosis.

Methods: A retrospective study will be conducted on CRC patients in colorectal surgery department at KHMC over the period from May 2014 to January 2018 with a total number of patients 247. We will refer to these patients' records in Princess Iman Center for Research and Laboratory Sciences to find their WBC count at presentation before surgery, then we will analyze the data to determine if there is any association between high WBC count and CRC and if there is a common findings among these patients.

Results: A 247 patients with CRC were studied, the age range was 19-85 years, 123 of the patients were males and 124 were females with a male to female ratio almost 1:1. WBC count ranged from $3.6 \times 10^3/\mu L$ to $21.2 \times 10^3/\mu L$. 43 patients had high WBC count (leukocytosis) which constitute about 17.4% of all patients. 22 of these 43 patients were males (51%) and 21 were females (49%).

Conclusion: CRC sometimes associated with increased WBC count, and this may affect the pattern of the disease in patients who have leukocytosis, further comprehensive studies are needed to confirm the effect of leukocytosis on prognosis and the role of WBC as an early screening marker for CRC patient.

Key words: Colorectal cancer, White blood cell, leukocytosis, inflammatory marker.

Introduction

Colorectal cancer is the third most common cancer in males and females in United States and western countries.[1,2] The incidence of CRC is increasing gradually with many factors affecting its incidence; mainly the family history of CRC, cigarette smoking, obesity, animal fats, alcohol intake, and sedentary lifestyle.[3] Chronic inflammation has been hypothesized to have a role in cancer pathogenesis.[3,4,5,6] CRCs are classified by etiology as inherited, inflammatory, and sporadic. The most common type is sporadic accounting for more than 80% of CRC.[7] It mainly occurs in the middle to late years of life with the mean age at diagnosis of 68 years.

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[8,9]Clinical findings in CRC patients depend on the site and size of tumor and the presence of complications including obstruction, perforation, and hemorrhage. Diagnosis is made through laboratory tests, imaging studies, and lower endoscopic procedure.[10] Screening for CRC aims to detect the disease in the early stages in which the disease is curable and has a favorable prognosis.[1,8] Screening starts with simple commonly used test which is fecal occult blood (guaiac test), if it shows positive results on two different samples then we proceed to structural screening.[9]Structural screening for CRC includes flexible sigmoidoscopy and colonoscopy.[1]Tumor markers which are serum proteins may help in screening for CRC but lack of sensitivity and specificity limits their use in screening, the most familiar marker is carcinoembryonic antigen (CEA) which is more applicable as prognostic marker and recurrence marker after surgery.[10,11]Sometimes inflammatory markers used in screening process of CRC because as we mentioned previously that there is a relationship between inflammatory conditions and cancers.[5] Chronic inflammation leads to chronic activation of the immune system and antigenic stimulation which play a role in development of cancer. Inflammatory bowel disease is a well-established cause of CRC. [3, 12]In the inflammatory conditions some markers are elevated in the blood such as C-reactive protein (CRP) and white blood cell count (WBC).[3,4]CRP is a protein produced by the liver in the inflammatory conditions.[13]WBC count is the circulating leukocytes that increase reactively in many conditions and considered a non-specific inflammatory marker.[3,4]
In this study we are trying to find if there is association between high WBC count and CRC in KHMC.

METHODS

In this retrospective study we referred to colorectal surgery department records in KHMC looking for patients diagnosed with colorectal cancer over the period from May 2014 to January 2018, the total number of patients was 247, they were primarily diagnosed with CRC by tissue biopsy through colonoscopy or recto-sigmoidoscopy, and they all underwent surgical resection of tumor with different open and laparoscopic procedures, histopathological types and grades were documented in lab reports for each patient. Then we referred to patients records in the laboratory to find their WBC count in the complete blood counts test (CBC) at presentation. Data analysis for these patients was performed to determine mainly the percentage of patients having high WBC count at presentation, and to find if there is any effect of their higher count on the disease outcome and if they have a difference in the Body Mass Index from other patients.
The cut-off point for normal WBC count is $11 \times 10^3/\mu L$ and the normal range for BMI is 18.5-24.9 kg/m^2, 25-29.9 kg/m^2 is overweight and above 30 kg/m^2 is obese.[14,15]

RESULTS

A total number of 247 patients with CRC were studied. The age range was 17-90 years with a median age of 54 years, the mean age of diagnosis is 58 years. About 91% of patients are above the age of 40 years. The M:F was almost 1:1 with 124 female patients and 123 male patients. The WBC count in their CBC test at presentation was ranging from 3.6-21.2x10^3/\mu L. Patients having high WBC count were 43 out of 247 (17.4%) with 22 of these patients were males (51%) and 21 were females (49%). The age range of the patients who were found to have high WBC count was 40-78 years. For the studied patients the body mass index ranges from 19 to 49 kg/m^2, with the median BMI=34 kg/m^2, 41% of patients have normal BMI, 38% have high BMI, and 21% are obese with very high BMI. The targeted patients who have high

WBC count was found to have higher BMI with 36% having normal BMI, 28% with high BMI, and 36% are obese. The site of tumors in our patients was colonic in 60% and rectal in 40%. In patients with leukocytosis the percentages differ and showed mainly colonic site in 77% and rectal in 23%. The patients with high WBC count do not show differences from other patients with normal count regarding type of surgery (open versus laparoscopic) duration of operation, hospital stay, oral intake post-op, complications after surgery, and readmission.

Table I. Characteristics of CRC patients with normal vs. high WBC

	Patients with normal WBC	Patients with high WBC
Age	17-90 years	40-78 years
Sex	M:F=1:1	M:F=1:1
BMI		
Normal	42%	36%
Overweight	40%	28%
Obese	18%	36%
Site of tumor		
Colon	56%	77%
Rectum	44%	23%

DISCUSSION

CRC was reported in some studies to be slightly more common in males with M:F=1.4:1.[16] In our study the incidence of CRC is almost the same in males and females, which is in concordance with Haggaret al.[17]In previous studies conducted on Jordanian patients the M:F was found to be 1.3:1 which means that the disease incidence is increasing in females in Jordan.[18,19]Regarding the age of patients 9% of our patients are below 40 years at time of diagnosis while in Iran a study conducted in 2005 on CRC patients revealed that about 17% of the patients were younger than 40 years while other studies suggested that 7% of their patients were younger than 40 years.[20,21]The mean age of diagnosis of CRC in our study group was 58 years while in US according to Surveillance, Epidemiology, and End Results(SEER) national cancer registry databasethe mean age CRC patients was 71 years which means that CRC presents at younger age in Jordan as our study and other previous studies on CRC patients in Jordan revealed.[18,19,22]

In this study we found that about 17.4% of patients with CRC have leukocytosis at their presentation, and upon analysis of the data of this group of patients we found that there are no differences in their operative and postoperative findings and complications but they were found to have older age range and higher BMI in comparison to the other group. This findings was also reported by Young Jae-Lee et al.[3]

We analyzed the BMI of the patients and found that 41% of them have normal BMI, 38% have high BMI (overweight), and 21% have very high BMI (obese), these BMI results was much lower than that found in North America by the National Surgical Adjuvant Breast and Bowel Project (NSABP).[23]In the targeted group who have leukocytosis the percentage of obese patients was higher than those who do not have leukocytosis, this may result from the possible association between obesity and reactive leukocytosis.[24] The explanation for this interrelation between obesity and leukocytosis is that adipocytes release proinflammatory cytokines in particularly IL-6 which cause increase in WBC count.[2] Regarding the site of tumor, our results was close to D.P.S.Sohalet al. who found that about 65% of patients have

colonic tumor and 35% have rectal tumor.[25] Leukocytosis in cancer patients usually is due to either infection or bone marrow metastasis, but in CRC, leukocytosis is also linked to inflammation in the large bowel that predispose to cancer.[3,12,26] In Salvenet al. leukocytosis in cancer patients was attributed to vascular endothelial growth factor (VEGF) which was produced by human tumor cells, while in other studies the WBC count was linked to increased risk of cancer.[27,28] A study conducted in Korea demonstrate that high WBC count is associated with increased the incidence and mortality of colon cancer.[3] Leukocytosis was linked to increased mortality because of its association with significantly increased risk of venous thromboembolism in cancer patients.[29]

Limitation of the study
We faced some limitations in our study. First, there was no documented history of the risk factors for CRC that patients have such as colorectal polyps and inflammatory bowel disease. Second, we could not find WBC count in our patient's records for the previous months before diagnosis of cancer and for the next months after surgery as follow up, so it was not possible to determine the chronicity.

Conclusion
CRC sometimes associated with increased WBC count, and this may affect the pattern of the disease in patients who have leukocytosis, further comprehensive studies are needed to confirm the effect of leukocytosis on prognosis and the role of WBC as an early screening marker for CRC patient.

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