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Incidence of Colorectal Carcinoma in Patients Undergoing Appendectomy After Age of 40 Years in Sulaimani Teaching Hospital

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Abstract

Background The appendiceal disease is one of the most common reasons for emergency hospital admission, and appendectomy is one of the most frequently performed emergency procedures. Obstruction of the appendiceal lumen is the usual cause of acute appendicitis. However, in elderly patients, it may also be due to a neoplasm of appendix, cecum, or even colorectal carcinoma and appendicitis can be its first manifestation. Of all the gastrointestinal tract malignancies, colorectal carcinoma is the most common one.

Objective To find the incidence of the carcinoma of colon in patients above 40 years of age who underwent appendectomy.

Methods Two groups of patients studied from Sulaimani Teaching Hospital and Kurdistan Center for Gastroenterology and Hepatology. Both groups underwent colonoscopy and one group only had appendectomy. Non-appendectomized group used as control. A 213 patients from a total of 545 patients studied from October 1st, 2018 to September 30th, 2019.

Results More than half of the patients (54%) had normal colonoscopy, others showed internal hemorrhoid (15.5%), polyp (15%), sigmoid mass (0.9%), rectosigmoid mass (0.5%) and gastrointestinal stromal tumor (0.5%). Histopathology results were tubular adenoma with low-grade dysplasia (36.4%), hyperplastic polyps (34.1%), adenocarcinoma (2.3%), and familial adenomatous polyposis (2.3%).

Conclusion The incidence of colorectal carcinoma is 4.76% in the studied group whom underwent appendectomy after 40 years of age.

Keywords Acute appendicitis, adenocarcinoma, colonoscopy, colorectal cancer, mucinous neoplasm of appendix, appendectomy.

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List of abbreviations: CRC = Colorectal carcinoma, CT = Computed Tomography, FAP = Familial adenomatous polyposis, GIST = Gastrointestinal stromal tumor, KCGEH = Kurdistan Center for Gastroenterology and Hepatology, SPSS = Statistical package for the social sciences, STH = Sulaimani Teaching Hospital, U/S = Ultrasound

Introduction

Colorectal cancer (CRC) is the most common gastrointestinal tract malignancy. CRC incidence reaches 10-fold variation throughout the world. Australia

and New Zealand have the highest incidence of 44.8 per 100,000 population in men and 32.2 in women; compared to Western Africa which has only 4.5 per 100,000 in men and 3.8 in women [1]. In the United States, there are over 140,000 new cases diagnosed annually and more than 50,000 fatalities each year, which ranks CRC as the third most lethal cancer in the United States [2].

In 2012, there were about 1.4 million new CRC cases and almost 700,000 deaths, however; it is predicted to grow by 60% to more than 2.2 million new cases and 1.1 million cancer deaths by 2030 [3].

CRC is more common with increasing age, and it is not so common before the fourth decade of life [4]. Nevertheless, lately, there has been a rise of CRC between the ages of 40 to 44 years [5].

Risk factors for developing CRC include aging, hereditary risk factors, environmental and dietary factors, and inflammatory bowel disease. Cigarette smoking, pelvic irradiation, and ureterosigmoidostomy are among other causes [6-8]. However, 70% of CRC are sporadic and minority is hereditary [8].

Most of the CRC develop from adenomatous polyps. Colorectal polyps can be classified as inflammatory (pseudopolyp, benign lymphoid polyp), hamartomatous (juvenile, Peutz Jeghers, Cronkite-Canada), hyperplastic and neoplastic (tubular adenoma, villous adenoma, tubulovillous adenomas, serrated adenomas/ polyps) [9].

It takes a decade for the adenoma-carcinoma sequence to develop. The majority of adenomas start as tiny polyps that grow and become dysplastic and at the end cancerous [10-11].

There are three categories of CRC screening including stool-based, imaging, and endoscopic tests. Stool-based tests such as the Guaiac-based fecal occult blood test and fecal immunochemical test can detect asymptomatic cancers at an early stage. Although they are not expensive and noninvasive but they are not capable of polyp detection and less sensitive for adenoma [12].

Imaging tests include double-contrast barium enema, computed tomographic colonography, and colon capsule endoscopy. The first two tests are capable of detecting polyps larger than 10 mm [13], while the latter is more expensive and cannot take biopsy.

Endoscopic tests include flexible sigmoidoscopy and colonoscopy. The distal gastrointestinal tract up to the splenic flexure can be visualized by the flexible sigmoidoscopy. But inability to visualize proximal colon makes it less sensitive. With colonoscopy, the entire length of the large bowel and distal small bowel can be visualized. It is considered the “gold standard” in screening CRC. It can visualize and take biopsy from cancerous and precancerous lesions. But it requires bowel preparation and sedation. Major complications include bleeding and perforation, which are more for therapeutic excisional biopsies.

The appendiceal disease is among the most common reasons for emergency hospital admission, and appendectomy is one of the most frequent emergency procedures performed. The lifetime risk of developing appendicitis is 8.6% for males and 6.7% for females, with the highest incidence in their twenties and thirties [14].

Classic physical findings such as pain and tenderness at McBurney's point, shifting pain from the central abdomen to right iliac fossa, anorexia, nausea, rebound tenderness, elevated temperature, leukocytosis, and shifting white blood cells to the left, have been used to make the diagnosis of acute appendicitis.

Pathologically, obstruction of the appendiceal lumen is the usual cause of acute appendicitis. However, in elderly patients, it may also be due to a neoplasm originating from appendix or cecum [15-17].

Ultrasonography (U/S) and computed tomography (CT) scan are the most commonly used imaging tests in patients with abdominal pain, particularly in the evaluation of possible

appendicitis. Multiple meta-analyses have been performed comparing the two imaging modalities. Overall, CT scan is more sensitive and specific than ultrasonography in diagnosing appendicitis. Imaging investigations like U/S and CT scan are increasingly used as a tool to exclude right-sided (non-appendiceal) colonic tumors on emergency admissions with clinical features of acute appendicitis especially in patients that are 40 years or older [18].

We suggest that if acute appendicitis is happening predominantly in young age population, and CRC is more common among middle and old age; then the patients present with a picture of acute appendicitis after the age of 40 may have CRC induced appendicitis.

Methods

This is a combined prospective and retrospective observational case series study conducted in Sulaimani Teaching Hospital (STH) between October 1st, 2018, and September 30th, 2019. Two groups of patients studied. We wanted to compare patients whom presented to emergency hospital and diagnosed as acute appendicitis and as a result of investigations or surgical operation CRC found; and to compare with a second group (control group) who didn't underwent appendectomy but underwent colonoscopy for other reasons.

Group A

Inclusion criteria

Includes 21 patients from a total of 86 patients who were above the age of 40 years and underwent appendectomy followed up for a duration of one to six months. They were contacted by phone three times (over a period of two months) to undergo colonoscopy. Only 15/21 patients were included.

Exclusion criteria

Patients who didn't respond, had no contact number, below the age of 40 years, or didn't want to do a colonoscopy were excluded.

Group B

Inclusion criteria

Data from Kurdistan Center for Gastroenterology and Hepatology (KCGEH) showed that the patients who were above the age 40 years and underwent colonoscopy were 198 patients from a total of 459 patients. Patients were contacted over the phone 3 times over a period of 3 months. Group B used as a control.

Exclusion criteria

Those who were below age of 40 years; didn't have contact number, didn't respond, have histopathology report of colonoscopy, or underwent colonoscopy after colorectal surgery, were excluded.

Figure 1 shows further details about the patients included in this study.

A questionnaire formulated and data regarding demography, age at the time of appendectomy, result of colonoscopy and histopathology, were collected.

Approval of ethics committee of University of Sulaimani, College of Medicine was granted on February 4th, 2020; number 108.

Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) software version 25. Incidence, p-value, and odds ratio were calculated. A p-value of 0.05 or less considered statistically significant.

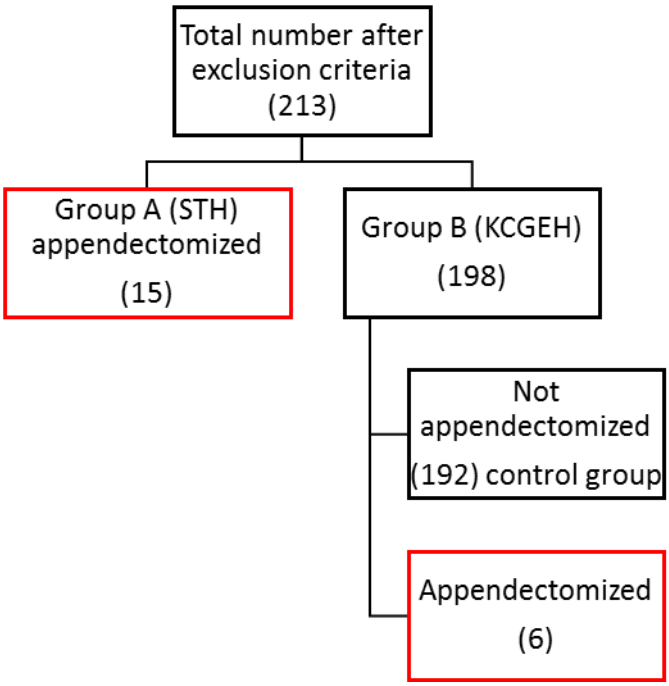

Figure 1. Flow chart of included patients. STH: Sulaimani Teaching Hospital, KCGEH: Kurdistan Center for Gastroenterology and Hepatology

Results

The mean age of patients in this study was 43±11.12 years with a range of 40-87. Females were 113 (53.1%) and males were 100 (46.9%). 21 patients (9.9%) underwent appendectomy and 192 patients (90.1%) were non-appendectomized as shown in table 1.

Table 1. General characteristics of patients

Variable		(mean±SD)	Range
Age (yr)		(43±11.12)	40-87
		Number	**Percentage**
Gender	Male	100	46.9%
	Female	113	53.1%
Appendectomy	Yes	21	9.9%
	No	192	90.1%

Table 2 shows the colonoscopic gross findings for the total 213 patients, and here are some of the findings: one patient (0.5%) had cecal mass, two patients had sigmoid mass (0.9%), one patient (0.5%) had rectosigmoid mass, one patient had gross finding, which confirmed later on biopsy to be gastrointestinal stromal tumor (GIST) (0.5%), 32 patients had polyp (15%), and 33 patients had internal hemorrhoids (15.5%). While 115 patients had normal colonoscopy (54%). GIST diagnosis was based on histopathological reporting from a tissue biopsy, which was taken during colonoscopy.

Table 2. Gross findings of colonoscopy

Colonoscopy (gross findings)	Number (Percentage)
Normal	115 (54%)
Internal hemorrhoid	33 (15.5%)
Polyp	32 (15%)
Diverticula	13 (6.1%)
Colitis	4 (1.9%)
Solitary Rectal Ulcer Syndrome	3 (1.4%)
Erosions	2 (0.9%)
Rectal nodularity	2 (0.9%)
Sigmoid mass	2 (0.9%)
Ileal ulcer	1 (0.5%)
Colonic ulcer	1 (0.5%)
Flat lesion	1 (0.5%)
Gastrointestinal stromal tumor	1 (0.5%)
Telangiectasia	1 (0.5%)
Rectosigmoid mass	1 (0.5%)
Cecal mass	1 (0.5%)
Total	213 (100%)

Histopathology assessment of the colonoscopy specimens (total 44 specimens) shows 16 patients (36.4%) had tubular adenoma with low-grade dysplasia, 15 patients (34.1%) had hyperplastic polyps, 1 patient (2.3%) had mucinous neoplasm of appendix with low-grade dysplasia, 1 patient (2.3%) had adenocarcinoma, and 1 patient (2.3%) had familial adenomatous polyposis (FAP). Normal colonoscopies, internal hemorrhoids, diverticula, and other conditions when no biopsy was taken, were not included in table 3.

Table 3. Results of histopathology of specimens taken during colonoscopy

Colonoscopy (Histopathology)	Appendectomized Number (Percentage)	Non-appendectomized Number (Percentage)	P value
Hyperplastic polyp	3 (42.9%)	12 (32.4%)	
Tubular Adenoma, Low grade dysplasia	2 (28.6%)	14 (37.6%)	
Colitis	0 (0%)	6 (16.2%)	
Familial adenomatous polyposis	0 (0%)	1 (2.7%)	0.288
Adenocarcinoma	0 (0%)	1 (2.7%)	
Data not available	1 (14.3%)	3 (8.1%)	
Mucinous neoplasm of appendix, low grad dysplasia	1 (14.3%)	0 (0%)	
Total	7 (100%)	37 (100%)	

Total number of patients with appendectomy was 21 (15 from group A, and 6 from group B). There was only one patient with mucinous neoplasm of appendix (Figure 1).

$$\frac{munious\ neoplasm}{Group\ A(15)+group\ B(6)} = \frac{1}{15+6} x100 = 4.76\%$$

Thus, the incidence of colorectal cancer among appendectomized patients is 4.76%.

Total number of patients without appendectomy was 192 (Group B). There were 2 patients with CRC (one patient with adenocarcinoma and one patient with FAP). (Figure 1).

$$\frac{FAP+adenocarcinoma}{Group\ B(192)} = \frac{2}{192} x100 = 1.04\%$$ Hence,

The incidence of colorectal cancer among non-appendectomized patients is 1.04%.

Mucinous neoplasm, FAP and adenocarcinoma from table 3 and patient numbers from figure 1 are used to calculate table 4. Details of the calculations are shown above.

Table 4. Incidence of carcinoma of colon among appendectomized and non-appendectomized patients

Data	Incidence of carcinoma of colon
Appendectomized	4.76%
Non-appendectomized	1.04%

Discussion

In this study, the mean age of appendectomy is 54 years, this is consistent with a study done by Khan et al. [19]. The majority of colonoscopies showed normal findings. The most common other colonoscopy findings were internal hemorrhoids and polyps (Table 2).

Female to male ratio is 1:1.13 while it was 1:1.06 in a similar study by Khan et al. [19].

One patient (14.3%) from appendectomized group A had low-grade mucinous neoplasm of appendix. Appendiceal mucinous neoplasm is rare dysplastic mucinous tumor, based on their cytologic features can be further classified into low-grade or high-grade. Diagnosed incidentally and clinical presentation is not specific. Low-grade appendiceal mucinous neoplasms don't invade the epithelium of appendix, but because they can grow into the muscularis propria, they can irritate and cause inflammation of the appendix, and can even cause the appendix to rupture. The best treatment for low-grade appendiceal mucinous neoplasms that are intact and confined to the appendix is an appendectomy. But if ruptured, spreading neoplastic cells through the peritoneum, leads to pseudomyxoma peritonei [20,21].

Two patients (28.6%) from appendectomized group A and 14 patients (37.6%) from nonappendectomized group B had tubular adenoma with low grade dysplasia. These tumors are classified as the low-risk group, which includes patients with 1-2 tubular adenomas of less than 10 mm with low grade dysplasia. Based on recommendations of the European Society of Gastrointestinal Endoscopy, it requires participation in national screening programs 10 years after the index colonoscopy. If no screening program is available, repetition of colonoscopy 10 years after the index colonoscopy is recommended [22].

It's well known that the adenoma-carcinoma sequence is a major role in the development of CRC [23,24]. In a study by Atkin and colleagues, they found out that colonoscopy surveillance was associated with a noticeable reduction in the incidence of CRC in the intermediate and high-risk adenomas compared with no surveillance [25].

Three patients (42.9%) from appendectomy group A and 12 patients (32.4%) from nonappendectomy group diagnosed with hyperplastic polyp. Hyperplastic polyps are the most common type of colorectal findings. They are considered to be benign tumors. In a study by Laiyemo and colleagues [26], they didn't find a strong relationship between hyperplastic polyps and recurrence of adenomatous polyps. Therefore, the current guidelines for surveillance colonoscopy is after 10 years, this resembles the same guidelines for the patients without any polyps.

Obstruction of the lumen of the appendix is the most common cause of appendicitis. Backpressure from CRC may cause inflammation of the cecum and occlusion of the appendix [8]. Acute appendicitis can also develop through inflammation and edema of appendiceal wall or as a consequence of obstruction of its lumen. Another pathology is immune mediated lymphoid hyperplasia of malignancy resulting in obstruction of the lumen of appendix [27].

Our results show that incidence of CRC among appendectozied patients is 4.76%, while among non-appendectomized (control group) patients is only 1.04. This means patients whom undergo appendectomy after age of 40 years are more likely to develop CRC.

Statistical analysis of group A and group B using SPSS software done and odds ratio calculated. An odds ratio is a measure of relationship between exposure and outcome. It is most commonly used in case-control studies; however, they can also be used in cross-sectional and cohort study designs [28].

The results of the present study were an odds ratio of 2.4. This means incidence of CRC among appendectomized patients is 2.4 time higher. In a study of 1873 patients by Lai et al it was 38.5 [29].

This study is limited by some factors that include a single center experience, and the small number of colonoscopies in the appendectomized group. That small number of colonoscopies was due to the fact that the majority of patients either refused colonoscopy, mostly due to their histopathology results that didn't mention malignancy, or they had job restriction in the morning, or they were afraid that the investigation might find a tumor.

The absence of electronic medical records was another obstacle. Every patient had to be contacted and asked for their history, investigation papers, and follow up. We contacted 71 appendectomized patients to undergo colonoscopy but only 21agreed.

In fact, one of the patients who underwent colonoscopy was a 45-year-old female housewife who became anxious after our phone call, she consulted two general surgeons because she was afraid that we might have found some malignant pathology. Later she became so anxious that her family consulted a psychiatrist who put heron anxiolytic medication.

The current study found that the incidence of colorectal carcinoma is 4.76% in the studied group whom underwent appendectomy after 40 years of age, while among non-appendectomized (control group) patients is only 1.04.

Postoperative colonoscopy within 3 months is of diagnostic significance for smaller polyps and colorectal tumors.

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Author contribution

Dr. Abdulla: created the study and carried out the design, data curation, analysis, interpretation of data, writing the draft and critical revision under supervision of Dr. Faraj. Histopathological reporting of tissue biopsies carried out by Dr. Abdulqader. Follow up of the patients done by Dr. Mardan, Dr. Mohammed, Dr. Mahmood, Dr. Hussein and Dr. Shareef. All authors read and approved the final manuscript.

Conflict of interest
None to declare.

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