

Pathological study of colorectal cancer in Missan province

ABSTRACT

Aims: Colorectal cancer (CRC) is a major cause of morbidity and mortality in the worldwide and also ranks as the fifth-leading malignancy and death in Iraq. This study aimed to provide a present outlook of colorectal diseases among patients with special emphasis on histopathological changes associated CRC in Missan province in Iraq. **Methods:** This study was covered the period between (First April – 2015 to First October -2015) and all patient's data were collected from (50) patients aged between (40 -80 or more) with colon and rectal cancer on basis of age, gender and histopathological diagnosis in AL-Sadder hospital in Missan province. **Results:** Colorectal tumors observed high incidence with ages between (51-60) years old represented by (40 %) cases, while the lowest incidence observed in ages between(40 -50)years in percentage(12%)cases, CRC were more commonly found in men 28(56%)than women 22(44%) in (P < 0.05). Histopathological examination of the tissue specimens show the commonest type of colorectal cancer was Adeno carcinoma in the colon 22(44%) cases, Ulcerative colitis in the colon were represented by 10(20 %) cases, Mucinoid adenocacinoma were found in 8(16 %) cases, P eutz –jeghers syndrome were found in 3(6%) cases, and Lymphoma in the colon (Lymphoplasmocyte) observed in 7(14 %) cases. In conclusion the incidence of CRC was common in age older than fifty years in this study, commonest type of CRC was adenocarcinoma in colon, and the ulcerative colitis in chronic stage may lead to hyperplastic to the epithelial cells in colon. **Conclusion:** Proper implementation of preventive measures such as changing lifestyle factors might enhance control of colorectal disease.

Keywords: *Colorectal cancer, Missan province, Adeno carcinoma, Ulcerative colitis*

1. INTRODUCTION

Colon cancer (CRC) represents 15% of worldwide malignancies and third cause of cancer in men (10% of total) and the second cause of cancer in women after breast cancer (9.4% of total). Every year there are registered around one million new cases and 500 000 deaths caused by CRC worldwide. Incidence rates are similar between men and women with cancer of the large bowel and higher for males with rectal cancer, but the overall incidence of CRC is higher in males (sex *ratio* M:F = 1.4/1) [1]. The term colorectal cancer refers to a malignant growth anywhere along the colon and rectum and these cancers can also be referred to separately as colon cancer or rectal cancer depending on where they start [2]. The etiology is not known, CRC is considered a multifactorial disease, an important role being attributed to the impact of environmental factors on a genetically prone land. Hereditary predisposition is considered an important factor in colorectal carcinogenesis, although 80% of colorectal neoplasms occur in the absence of a family history of CRC [3].

A hypercaloric diet, high in fat and low in dietary fiber is positively correlated with the CRC occurrence. Obesity, Western diet and lack of physical activity are common risk factors for both type 2 diabetes mellitus and for CRC [4].

Smoking status, obesity, diabetes, physical activity, and high intake of alcohol were significantly associated with CRC, but only among subjects less adherent to the

Mediterranean diet(MD). MD was associated with a less detrimental effects of several health-related characteristics associated with CRC, and suggesting potential benefits of adherence to this dietary pattern with regards to CRC risk factors [5].

Ulcerative colitis and Cohn's disease are also considered risk factors for CRC [6]. The highest rates of the disease are seen in industrialized countries such as the USA, Europe, Australia and New Zealand. The lowest incidence is seen in non- industrialized countries as India and Algeria [7]. Epidemiological studies have revealed a number of risk factors for colorectal cancer including the age and the younger adults can develop colorectal cancer but the chances increase markedly after 50 age, where 9 out of 10 patients were diagnosed with colorectal cancer are older than 50 years .The men are more likely than the women to develop the colorectal cancer [8].

Genetic mutations may play role in 10% of colorectal cancer cases. One of these genetic mutations is called Familial Adenomatous Polyposis (FAD) which can cause hundreds or thousands of polyps to develop in the colon from every young age [9 & 10]. The diet with high red meat (beef, lamb, liver), and processed meats such as cooking meat at very high temperatures (frying, broiling, grilling) where many greatest chemicals that might increase colorectal cancer risk, also the low fiber diet have implicated to increasing the risk of colorectal cancer because it lead to decreased stool bulk and longer time for stools to remain in the large intestine, thus exposed the mucosa layer to toxins in the stool for longer periods of time.

CRC is more commonly located in the sigmoid and rectum, and there are two major histological types of CRC tumors consist of epithelial and mesenchymal tumors [11]. For uniformity and consistency in reporting, internationally accepted and used classification is that proposed by the WHO: adenocarcinoma, medullary carcinoma, colloid adenocarcinoma, „signet ring" squamous cell carcinoma, epidermoid carcinoma, adenosquamos, small cell carcinoma, undifferentiated carcinoma and other types [12]. Histopathological reporting of colorectal cancer provides important information both for the clinical management of the affected patient and for the evaluation of health care as a whole. In this study, we present the findings to detect the relationship between the age and increasing of colorectal cancer, also determined the commonest types of colorectal cancer.

2. Material and methods

The study was performed between (First April – 2015 to First October -2015) and all patient`s data were collected from (50) patients aged between (40 -80 or more) infected with colon and rectal cancer on basis of age ,gender and histopathological diagnosis ,were performed after surgical operations f in AL-Sadder hospital in Missan governorate. The tissue samples were kept in Buffered Formaldehyde (10%) for period (72) hours and after that the samples were treated according to the Luna [13] method for histopathological examination and stained with Hematoxylen –Eosin stain.

Statistical analysis. The data were analyzes by using Chi –Square in ($P < 0.05$)

3. Results

The data that were collected from the patients with colorectal tumors in ages between (51-60) years old which represented by (40 %) cases, followed by the ages between (61-70)years old (26%) cases , while the lowest incidence observed in ages between(40 -50)years in percentage(12%)cases, (Figure1). The total number of the men with colorectal cancer was 28(56%) cases, and the women 22(44%) cases of the all patients as shown in (Figure 2).

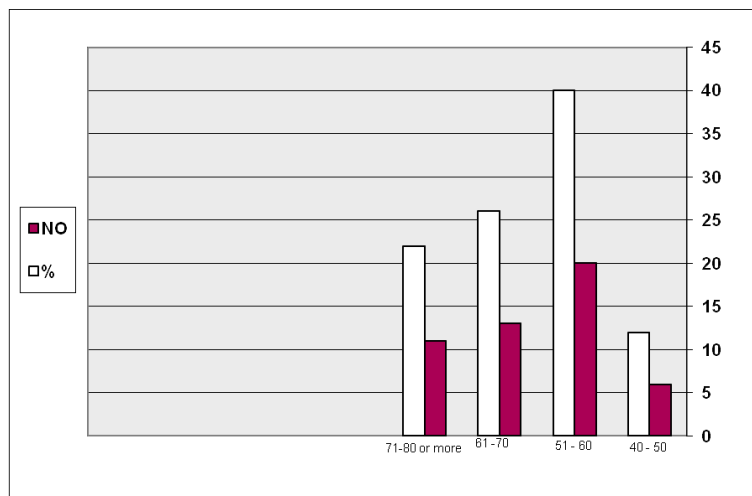
Histopathological examination of the tissue specimens that obtained from the patients with colorectal cancer through and after surgical operations show that the commonest type of colorectal cancer was the Adeno carcinoma in the colon represented by 22(44%) cases

79 (Figure 3) , and characterized by ability of the tumor cells to invade the wall of the colon and
 80 penetrated the colonic tissues ,the malignant glands infiltrate in the muscularis layer , also
 81 there is an area of necrosis within the large mass of tumor cells (Figure 4).

82 Ulcerative colitis in the colon were represented by 10(20 %) cases ,where the lesions were
 83 found in the mucosa layer which appear intensively hyperemic with considerable dilation of
 84 small blood vessels, also there are eosinophilic secretions and cells fragments with pus like
 85 materials filled the lumen of the glands (Figures 5&7).

86 Mucinoid adenocarcinoma were found in 8(16 %) cases and the lesion characterized by
 87 present large glandular structures with pools of extracellular mucin ,also shows a numbers
 88 of lymphocytes in the tissues around the glands , the nuclei in the small glands are round
 89 and fairly regular, (Figures 6&8).

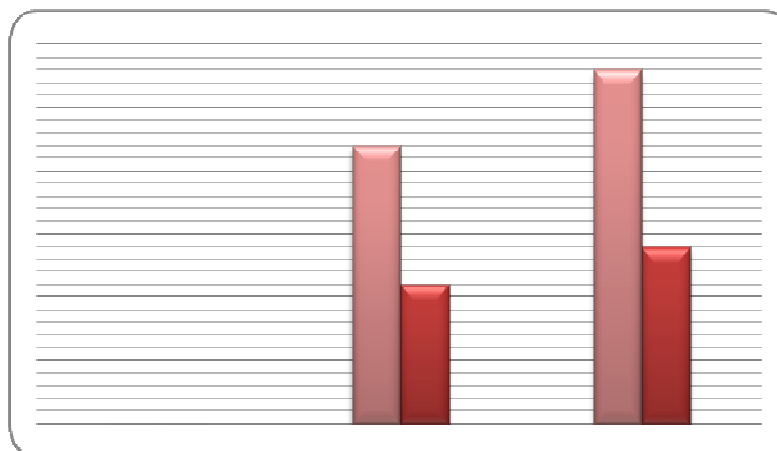
90 P eutz –jehgers syndrome were found in 3(6%) cases and the lesion characterized by
 91 present a numbers of lymphocytes in the tissues around the glands , the nuclei in the small
 92 glands are round and fairly regular (Figure 9). Lymphoma in the colon (Lymphoplasmocyte)
 93 observed in 7(14 %) cases, which shows small and rounded tumor cells with basophilic
 94 nuclei and scanty cytoplasm (Figure 10).
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96

97 **Figure (1):** Distribution of colorectal cancer among the patients according the different ages.

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Figure (2): Gender distribution of colorectal cancer diseases.

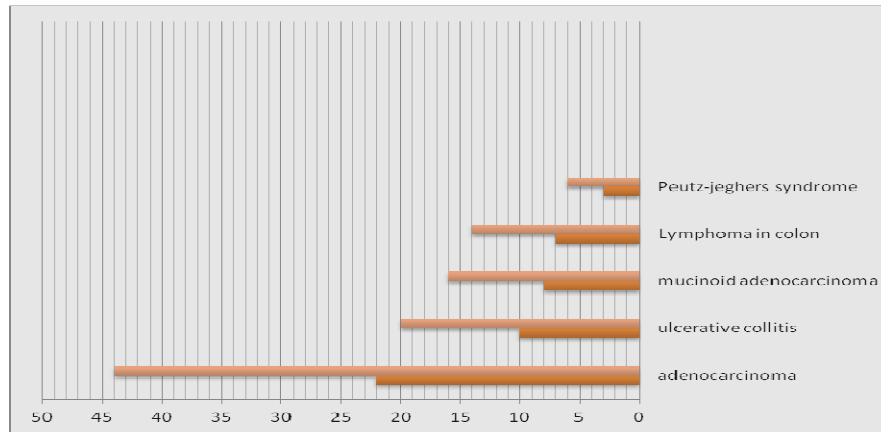


Figure 3: The commonest types of colorectal cancer and chronic inflammation in the colon that observed in this study

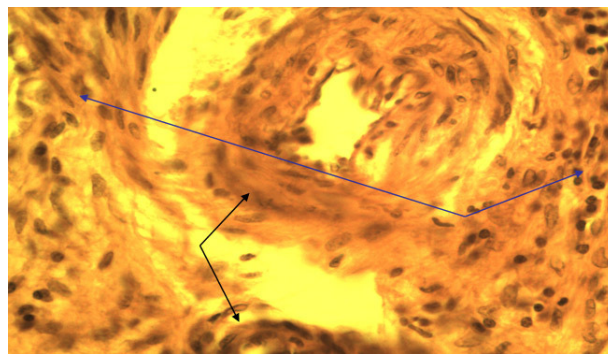
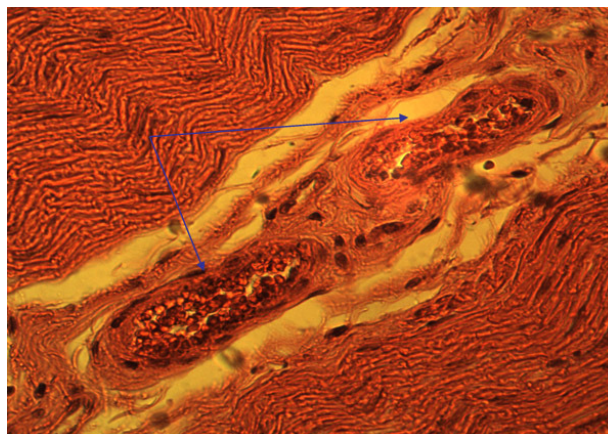
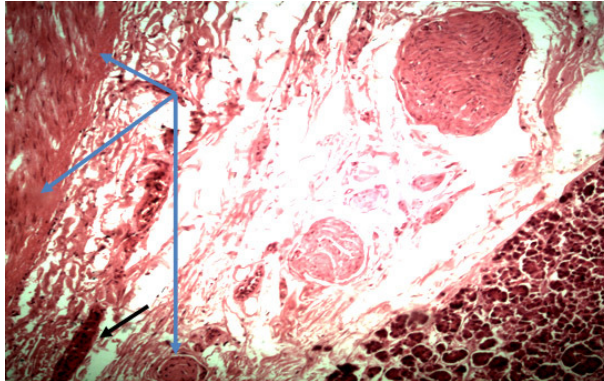


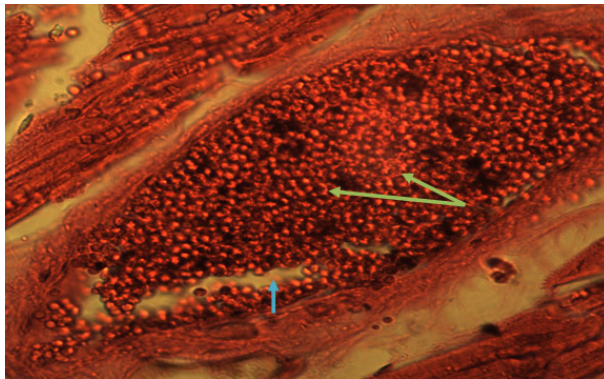
Figure 4: Adenocarcinoma in the colon: Characterized by presence tumor cells invade wall of the colon malignant glands → infiltrate in the muscularis layer → (HE.500).



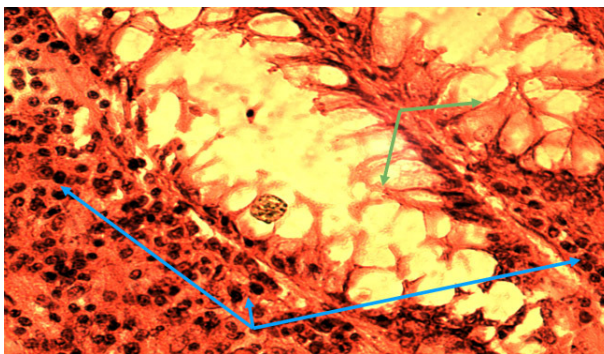
112 **Figure 5:** Adenocarcinoma in the colon: Shows numerous of cysts —→ surrounded by
113 thick layer of stroma (HE.500).



114
115 **Figure 6:** Ulcerative colites in the colon: Appear intensive hyperemic in mucosa layer —→
116 with dilation of B.V with pus like materials in the lumen of glands —→ (HE.500).



117
118 **Figure 7:** Ulcerative colitis in the colon: Shows eosinophilic secretions and cells fragments —→
119 with pus like materials filled the lumen of the glands —→ (HE.500).



122
123
124 **Figure 8:** Mucinous adenocarcinoma in the colon: shows large glandular structures with
125 pools of extracellular mucin —→ with numbers of lymphocytes around the glands —→
126 (HE.500).

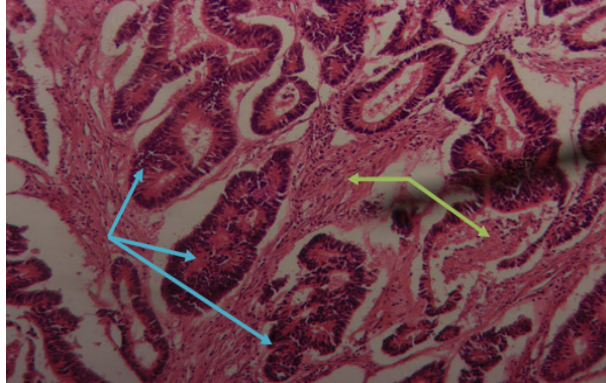


Figure 9: P eutz –jeghers syndrome in colon: composed of proliferative epithelium → ,stroma and smooth muscle arranged in arborizing pattern → (HE.125).

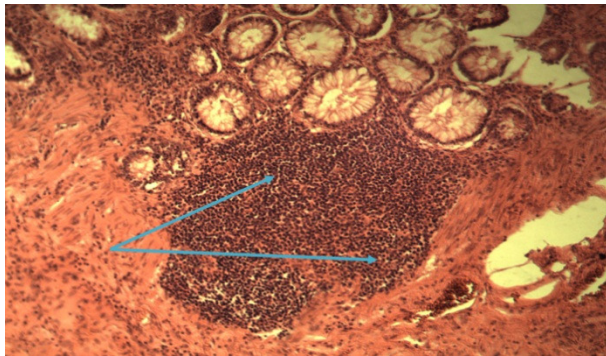


Figure 10: Lymphoma in colon: composed of small and rounded tumor cells with basophilic nuclei and scanty cytoplasm → (HE.500).

4. DISCUSSION

The peak incidence of colorectal cancer was observed in ages between (51-60) years followed by the ages between (61-70).this results agreed with [14] that said the incidence of colorectal cancer most commonly between (60to 70) years of age and fewer than 20% of cases occur before the age 50years and the chance of getting the disease increase markedly after (50)years where more than (9 out of 10) people diagnosed with colorectal cancer were older than (50) years .

Bull *et al* [15] were found the colorectal tumors occur in patients age older than sixty, where as non colorectal tumors occure in patients age under sixty and colorectal cancer characteristics occur in patients age older than sixty whereas benign colorectal tumors occur in patients age under sixty years. Admission rates of CRC patients in Thailand showed an increase with age and the highest rate was observed in those sixty years and older [16]. This retrospective study, showed that if the patient's age at diagnosis was more than sixty they developed more colorectal tumor features compared to non-colorectal tumor phenotypes which might begin from changing of no dysplasia of the cell progressing to indefinite dysplasia, low-grade dysplasia, high-grade dysplasia and finally to invasive adenocarcinoma [17].

153 Patient's older than sixty years old developed more CRC features compared to benign
154 colorectal tumors which is supported by several studies that CRC can arise from mucosal
155 colonic polyps including two most common histological types, hyperplastic and adenomatous
156 polyps [18].

157 Biondi *et al* [19] were refereed that the prevalence of elderly subjects with CRC is expected
158 to grow in the next future decades due to the increase of age in the general population. In
159 fact, CRC is infrequently diagnosed before age of 40, with a highest risk around age of
160 70.75% of CRC are identified in patients aged 65 years or older. In both Europe and United
161 States approximately 50% of CRC patients are older than 70 years of age and in this age
162 group CRC is the second most common cause of cancer death. Thus, age could be
163 considered as a major risk factor for the development of colorectal cancer .Also added the
164 older patients being less likely to receive recommended therapy and elderly subjects should
165 receive screening and earlier diagnosis; the management of CRC should be more
166 aggressive and closer to that received by younger patients.

167 The colorectal cancer was observed most commonly in men than the women in this study .
168 Gender distribution of colorectal tumors were more present in males than the females and
169 CRC consider the second types in males after lung cancer and third to cervix and breast
170 cancer in women [8].

171 Bull *et al* [15] said that the colonic cancer has an equal age/sex distribution, but the rectal
172 carcinoma is more common in men , the reasons for this sex difference remain unclear ,but
173 the differences in exposure to the risk factors between the males and females may therefore
174 explain the varying sub site distribution of colorectal cancers observed between sexes.

175 Histopathological examination showed that the commonest type of colorectal carcinoma was
176 the adenomatous carcinoma in colon and the tumor took the form of un-ulcer with rolled
177 edge ,the mucosa layer seen in normal which continuous with thicker and basophilic of
178 malignant epithelium. There is a raised mass of tumor cells inside the rolled edges of crater
179 ulcer, the floor of the ulcer consist of carcenomatous tissue and malignant cells have
180 invaded down- wards and destroyed the muscular layer and invade the fatty tissues [15].
181 These results agreed with [18] that reported more than 95% of colorectal cancer is
182 adenocarcinoma, these cancer start in the cells form the glands make the mucus which
183 lubricate inside the colon and rectum. Also agreed with [16] were found adenocarcinoma in
184 (329/338) in percentage (97.3%), diffuse type (1/338, 0.3%), adenocarcinoma insitu (2/338,
185 0.6) and lymphoma (1/338, 0.3%).

186 The most common site lesion of CRC was in the colon which was commoner than rectal and
187 recto-sigmoid site lesions similar to other studies where the highest incidence rate of CRC
188 was found in the colon site [19, 20]. Adenocarcinoma was the most common type of CRC
189 found. It has a relatively better prognosis than other gastrointestinal malignancies such as a
190 mucinous and signet-ring cell carcinoma types which have a poorer prognosis [21].

191 Adenomatous carcinoma grossly maybe found in two types , enucleated (attached by a
192 narrow base and along stalk)or sessile (attached across aboard , flat base with no stalk)
193 .Histologically the adenomatous carcinoma may be tubular which composed tubular glands
194 extending downward from the outer surface of the mucosa , villous (composed of finger like
195 epithelial projections extending out ward from the surface of the bowel mucosa) , or both
196 (tubulovillous)and the villous are more likely to contain invasive carcinoma than are tubular

197 carcinoma [22]. More than 90% of colorectal carcinomas are adenocarcinomas originating
198 from epithelial cells of the colorectal mucosa [15].

199 Ulcerative colitis in the colon was represented by (10) of all cases. The ulcerative colitis is
200 inflammatory process can affect the colon and rectum but, limited to the mucosa and sub
201 mucosa layers in compared with Crohn's disease [23]. Grossly the colonic mucosa slightly
202 red and have extensive broad base ulcers. The chronic lesion may be lead to mucosal
203 atrophy with flat and smooth mucosal surface that lack the normal folds [24]. The ulcerative
204 colitis characterized by inflammation and ulceration with intensely hyperemic of the mucosa
205 layer, which combined with infiltration of inflammatory cells which is particularly intense in
206 the region of the muscularis mucosa [25].

207 In severe cases the extensive mucosal destruction may be accompanied ulcers that extend
208 more deeply in to the sub mucosa, but the muscularis and serosa are rarely

209 involved. In several epidemiological studies, many colorectal diseases were associated with
210 CRC such as an ulcerative colitis and inflammatory bowel disease [26; 27]. Those diseases
211 might be caused by an inflammation process which could promote colon tumor genesis by
212 various molecular mechanisms [23]. Oxidative stress and oxidative cellular damage that
213 occur in the process of inflammation were other important features that activate phagocytic
214 activity of leukocytes resulting in enhanced production of pro-oxidant molecules which can
215 pave the way for CRC [28]. Muroid adenocarcinoma was observed in (8) patients of all
216 cases. Muroid adenocarcinomas are the second most common type of cancer (about 5%)
217 and are diagnosed when mucus occurs in more than 50% of tumor tissue [29].

218 Longo *et al* [30] reported Muroid and Signet – cell tumors present more peritoneal
219 spreading, infiltrating through all layers of intestinal wall, more lymphoid involvement, greater
220 frequency of advanced stage of disease, a lower rate of curative resection, and lower overall
221 5-years survival rats. Muroid adenocarcinoma typically shows large glandular structures
222 with pools of extracellular mucin. Muroid adenocarcinoma occurs in patients with hereditary
223 nonpolyposis colorectal cancer (HNOCC or lynch syndrome) and represents high level MSI
224 tumors [31].

225 Peutz –jehgers syndrome were found in (3) cases and the lesion characterized by present
226 a numbers of lymphocytes in the tissues around the glands. Peutz Jeghers syndrome is a
227 rare familial disease first described by Peutz in 1921 and Jeghers in 1949; it is autosomal
228 dominant disorder present with multiple gastrointestinal hamartomatous polyps and
229 mucocutaneous hyper pigmentation [32]. Jeghers syndrome are most commonly seen in the
230 small intestine ,but can also occur in the colon, they are composed of proliferative epithelium
231 ,stroma and smooth muscle arranged in arborizing pattern [25]. Microscopically JPS have
232 distinctive histological appearance which show tree like branching and becoming
233 progressively thinner as they reach the polyps surface and covered by the mucosa native to
234 the region, heaped in to folds producing villous pattern [31]. Lymphoma in the colon
235 (Lymphoplasmacyte) observed in (7) of all cases. Lymphomas account for only 15 to 205 of
236 gastrointestinal lymphomas, a lower rate of involvement than either stomach (50 to 60%) or
237 small intestine (20 to 30%). Colorectal lymphoma is a rare condition and made up only 0.2%
238 of colonic malignancy, the colon and rectum are uncommon sites for lymphoma even
239 compared with other gastrointestinal sites, where the stomach and small bowel are
240 predominant for lymphoma [22]. The CRC in our country deserves a great awareness as a
241 public health issue. In the beginning, a cancer registry and a program of CRC prevention
242 have to be operational. Public education about early diagnosis can improve the prognosis of
243 CRC in our country[33].

244 5. Conclusion:

245 The incidence of CRC was common in age older than fifty years, the disease was observed
246 most commonly in men than the women in this study, the commonest type of CRC was

247 adenocarcinoma in colon, and the ulcerative colitis in chronic stage may lead to hyperplastic
248 to the epithelial cells in colon.

249 **6. Recommendations:**

250 Specific prevention programs should aim to promote lifestyle modification and change in
251 dietary habits such as increasing physical activity, reducing consumption of red meat, fresh
252 red meat, and cessation of cigarette smoking to promote better life for people.

253

254 **CONSENT**

255 It is not applicable.

256 **ETHICAL APPROVAL**

257 Ethical approval was obtained from Al-Sadder Teaching Hospital and the study was
258 performed in Department of pathology , confidentiality was maintained through out the
259 research period.

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- 337 has been used as an indirect marker of oxidant-induced cell injury [21].