Original Research Article

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

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

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

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

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

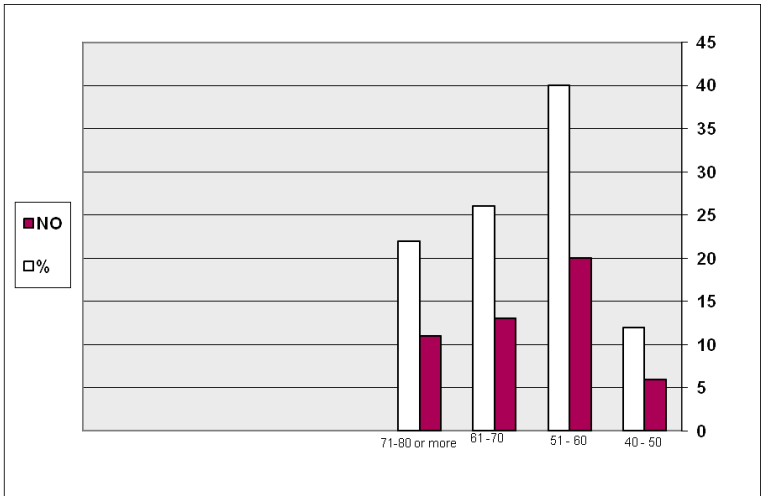

Figure (1): Distribution of colorectal cancer among the patients according the different ages.

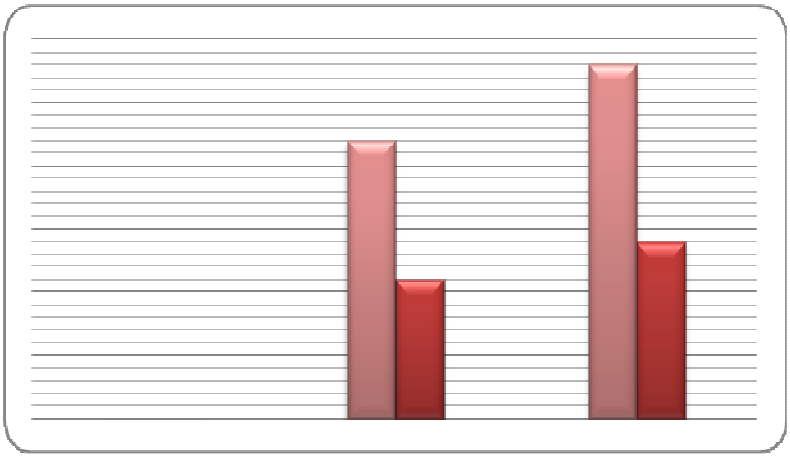

Figure (2): Ginder distribution of colorectal cancer diseases.

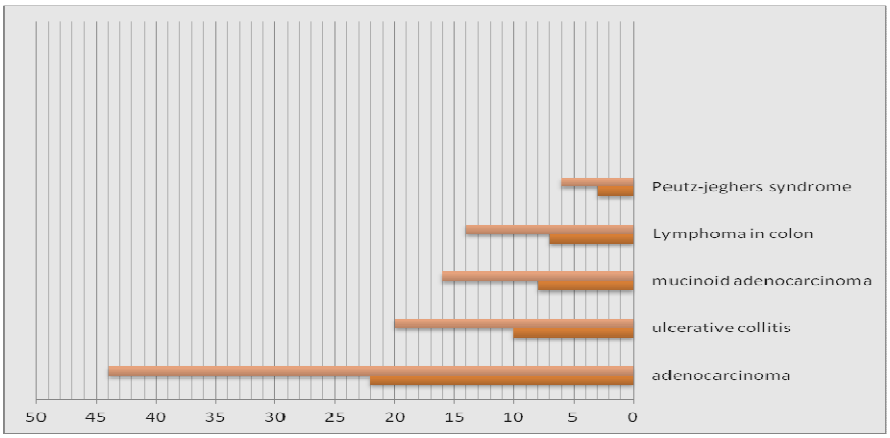

Figure 3: The commonest types of colorectal cancer and chronic inflammation in the colon that observed in this study

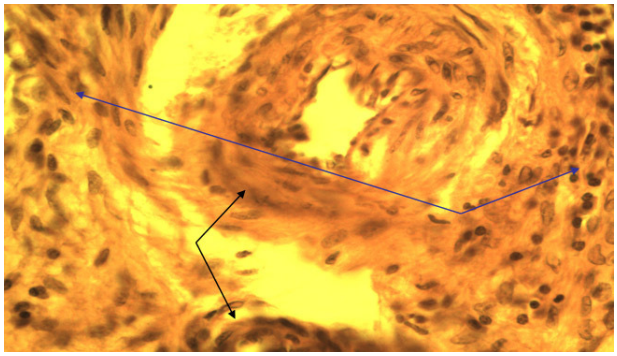

Figure 4: Adenocarcinoma in the colon: Characterized by presence tumor cells invade wall of the colon malignant glands → infiltrate in the muscularis layer → (HE.500).

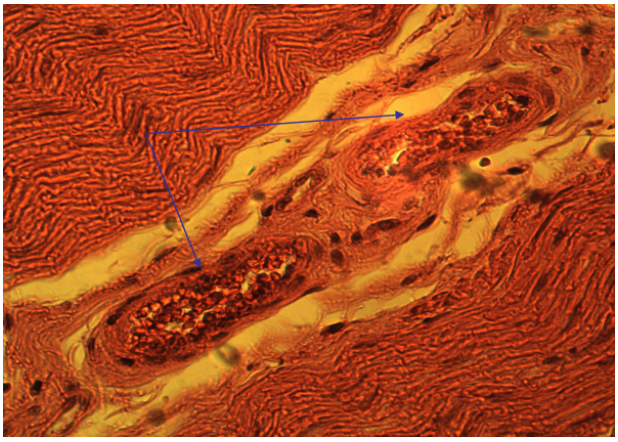

Figure 5: Adenocarcinoma in the colon: Shows numerous of cysts ⟶ surrounded by thick layer of stroma (HE.500).

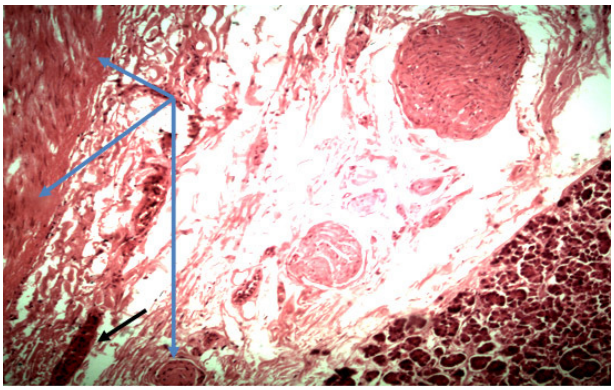

Figure 6: Ulcerative colites in the colon: Appear intensive hyperemic in mucosa layer ⟶ with dilation of B.V with pus like materials in the lumen of glands ⟶ (HE.500).

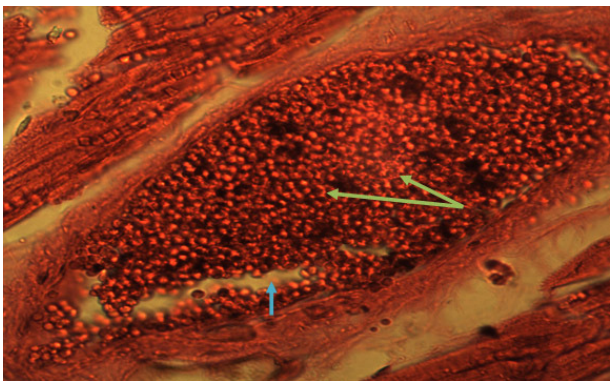

Figure 7: Ulcerative colitis in the colon: Shows eosinophilic secretions and cells fragments ⟶ with pus like materials filled the lumen of the glands ⟶ (HE.500).

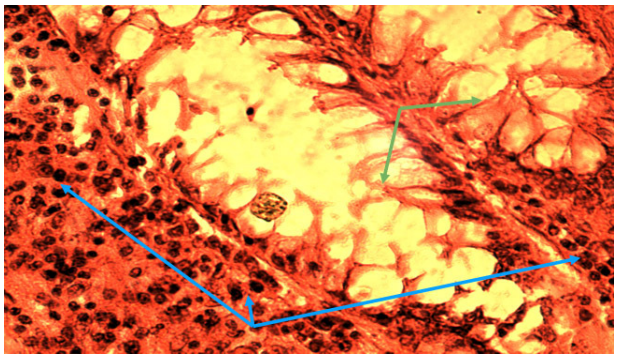

Figure 8: Mucinous adenocarcinoma in the colon: shows large glandular structures with pools of extracellular mucin ⟶ with numbers of lymphocytes around the glands ⟶ (HE.500).

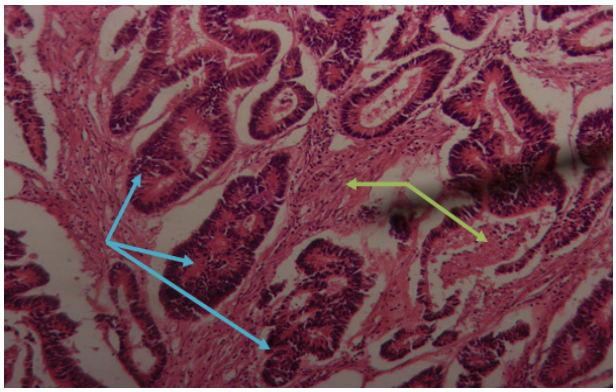

Figure 9: P eutz –jeghers syndrome in colon: composed of proliferative epithelium ,stroma and smooth muscle arranged in arborizing pattern (HE.125).

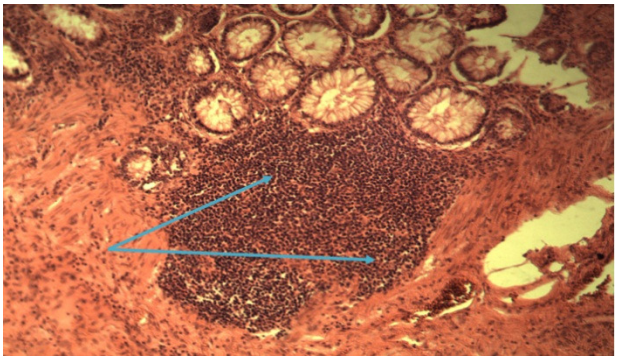

Figure 10: Lymphoma in colon: composed of small and rounded tumor cells with basophilic nuclei and scanty cytoplasm (HE.500).

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 characristics 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]**.

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

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

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

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

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

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

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

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

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

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

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

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

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

5. Conclusion:

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

6. Recommendations:

Specific prevention programs should aim to promote lifestyle modification and change in dietary habits such as increasing physical activity, reducing consumption of red meat, fresh red meat.

CONSENT

It is not applicable.

ETHICAL APPROVAL

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

6. References

1. Center MM, Jemal A, Ward EM (2009). International trends in colorectal cancer incidence rates. Cancer Epidemiol Biomarkers Prev; 18(16):1688-94.

2. Fleming M, Ravula S, Tatishchev SF, Wang HL (2012). Colorectal carcinoma: pathologic aspects. J Gastrointest Oncol,; 3:153-73.

3. Lynch HT, Chapelle A. (2003). Hereditary colorectal cancer. *N Engl J Med* ; 348:919–932.

4. Dahm CC, Keogh RH, Spencer EA, Greenwood DC, Key TJ (2010). Dietary fiber and colorectal cancer risk: a nested case–control study using food diaries. J Natl Cancer Inst; 102:614–626.

5. Biondi A,Vacante M,Ambrosino I,Cristaldi E, Pietrapertosa G, Basil F.(2016) Role of surgery for colorectal cancer in the eldery .*World. GI Surg J*;27; 8(9) :606 –613.

6. Lucendo J.A., Guagnozzi D (2012). Colorectal cancer surveillance in patients with inflammatory bowel disease: What is new?. *World J Gast Endosc*. 2012; 16; 4(4): 108–116.

7. Boyle P, Leon ME.(2002) Epidemiology of colorectal cancer. Br Med Bull;64:1-25.

8. Kumar V, Cotran R, Robbins S. (1997). Basic pathology, 6th edition. Philadelphia, Pennsylvania, W.B Saunders Company.

9. Aarnio M, Sankila R, Pukkala E et al.(1999) Cancer risk in mutation carriers of DNA-mismatchrepair genes. Int J Cancer;81:214-18.

10. **Rabor, D. and Adedeji, O.A. (2009)** Colorectal Cancer in Nigeria: 40 Years on. A Review. *European Journal of Cancer Care*, **18**, 110-115.

11. Fleming M, Ravula S, Tatishchev SF, Wang H (2012). Colorectal carcinoma: pathologic aspects. *J Gast Onco*; 3:153-73.

12. Puppa G, Sonzogni A, Colombari R, Pelosi G (2010). TNM staging system of colorectal carcinoma: a critical appraisal of challenging issues. Arch Patho Lab Med ; 134(6):837-52.

13. Luna,L.G.(1968). Manual of histology stain method of armel force in statute pathology,3Ed.the back stone diction.Mc grow hill book. Comp New York and Sydney.

14 . Triantafillidis JK, Nasioulas G, Kosmidis PA (2009). Colorectal cancer and inflammatory bowel disease: epidemiology, risk factors, mechanisms of carcinogenesis and prevention strategies. *Anticancer Res*, **29**, 2727-37.

15. Bull AD,Biffin AH, Mella JA,Radcliffe AG,William GT (1997). Colorectal cancer pathology reporting: aregional audit Jclin patho ;50:138 – 142 .

16. Kotepui M, Piwkham D,Songsri A (2013). Histopathological analysis of benigh colorectal disease and colorectal cancer in Hatyai hospital, Songkhla ,Thailand .APJ Cancer ,Vol 14.

17. Tsai CJ, Lu DK (1995). Small colorectal polyps: histopathology and clinical significance. *Am J Gastroenterol*, **90**, 988-94.

18. Zarchy TM, Ershoff D (1996). Risk of colorectal cancer in families of patients with adenomatous polyps. *N Engl J Med*, **334**, 1339-40.

19. Ji BT, Devesa SS, Chow WH, Jin F, Gao YT (1998). Colorectal cancer incidence trends by subsite in urban Shanghai, 1972- 1994. *Cancer Epidemiol Biomarkers Prev*, **7**, 661-6.

20 Grosso G, Biondi A, Galvano F, Mistertta A, Marventano S, Buscemi S,Drago F,Basile F (2014). Factors associated with colorectal cancer in the context of the Mediterranean Diet: A case control study . *J of Nutritional & Cancer*; 66 (4), 558-565.

21. Liu L, Lemmens VE, De Hingh IH, et al (2013). Second primary cancers in subsites of colon and rectum in patients with previous colorectal cancer. *Dis Colon Rectum*, **56**, 158-68.

22. Nozoe T, Anai H, Nasu S, Sugimachi K (2000). Clinicopathological characteristics of mucinous carcinoma of the colon and rectum. *J Surg Oncol*, **75**, 103-7.

23. Stefanescu LN.(2013). Clinical, histological and immune histochmical study of colorectal carcinoma .Doctoral thesis. Doctoral school, Uni Med Pharmacy .Craiova ; pp: 1 – 10 .

24. Ekbom A, Helmick C, Zack M, Adami HO (1990). Ulcerative colitis and colorectal cancer. A population-based study. *N Engl J Med*, **323**, 1228-33.

25. Risques RA, Lai LA, Brentnall TA, et al (2008). Ulcerative colitis is a disease of accelerated colon aging: evidence from telomere attrition and DNA damage. *Gastroenterology*, **135**, 410-8.

26. MatthewF,Ravula S,Wang L.(2012) Colorectal carcinoma :pathologic aspects .Patho. Dept, Med. JGO. California ,USA.

27. Eaden JA, Abrams KR, Mayberry JF (2001). The risk of colorectal cancer in ulcerative colitis: a meta-analysis. *Gut*, **48**, 526-35.

28. Winther KV, Jess T, Langholz E, Munkholm P, Binder V (2004). Long-term risk of cancer in ulcerative colitis: a population-based cohort study from Copenhagen County. *Clin Gastroenterol Hepatol*, **2**, 1088-95.

29. Roessner A, Kuester D, Malfertheiner P, Schneider-Stock R (2008). Oxidative stress in ulcerative colitis-associated carcinogenesis. *Pathol Res Pract*, **204**, 511-24.

30. Nesbakken A.(2014). History of colon and rectum cancer .Uni Hospt. Narway .

31. Longo R, Morabito A, Carillio G, et al (2006). Multiorganic dissemination of a colorectal signet ring cell carcinoma with fulminant clinical course. *Int J Gastrointest Cancer*, 37, 49-54.

32. Darré, T., Amégbor, K., Bagny, A., Sewa, E., Tchangai, B., Sakiye, A., Allasani, F., Bouglouga, O., Lawson, A.L. and Napo-Koura, G. (2014) Histo-Epidemiological Profile of the Colorectal Cancers in Togo. *Journal Africain d'Hépato- Gastroentérologie*, **8**, 226-229.

33 . Roncucci, L. and Mariani, F. (2015) Prevention of Colorectal Cancer: How Many Tools Do We Have in Our Basket? *European Journal of Internal Medicine*, **26**, 752-756.

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