

Colonic cancer: incidence, pattern & role of radical surgery in stage 11 AND 111, in Al Nassiryia

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ABSTRACT

Background:

Invasive colorectal cancer is a preventable disease. Early detection through widely applied screening programs is the most important factor in the recent decline of colorectal cancer in developed countries. Full implementation of the screening guideline can decrease mortality rate from colorectal cancer in the United States by an estimated additional 50%; even greater reductions are estimated for countries where screening tests may not be widely available at present. New and more comprehensive screening strategies are also needed.^[1] Fundamental advances in understanding the biology and genetics of colorectal cancer are taking place. This knowledge is slowly making its way into the clinic and being employed to better stratify individual risks of developing colorectal cancer, discover better screening methodologies, allow for better prognostication, and improve one's ability to predict benefit from new anticancer therapies.^[2] In the past 10 years, an unprecedented advance in systemic therapy for colorectal cancer has dramatically improved outcome for patients with metastatic disease. Until the mid-1990s, the only approved agent for colorectal cancer was 5-fluorouracil. New agents that became available in the past 10 years include cytotoxic agents such as irinotecan and oxaliplatin, oral fluoropyrimidines (capecitabine and tegafur), and biologic agents such as bevacizumab, cetuximab, and panitumumab. Though surgery remains the definitive treatment modality, these new agents will likely translate into improved cure rates for patients with early stage disease (stage II and III) and prolonged survival for those with stage IV disease. Further advances are likely to come from the development of new targeted agents and integration of those agents with other modalities such as surgery, radiation therapy, and liver-directed therapies.^[3] This study was done in Al Nassiryia in Al Hussein teaching hospital through 2 years from April 2008 to March 2010 with 3 years follow up on 32 patients complaining from stage 11 and stage 111 colonic cancer, 10 of them they arrived to the hospital as an emergency cases with intestinal obstruction or uncontrolled bleeding per rectum and 22 cases as an elective cases who presented from either sub acute intestinal obstruction, chronic loss of weight, chronic loss of appetite abdominal mass and or intermittent bleeding per rectum, ages of patients range between 30 to 80 years. 18 patients males and 14 patients were females. Aim is To make screening for stage 11 & 111 colonic cancer admitted to our unit and role of radical surgery in

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emergency cases comparing with radical surgery in elective surgery . Ca. of rectum was excluded from the study. We get 84%(27 patients) above 50 years, males were more,18 patients, annular type were the commonest type (50%). , about histopathological study 18 patients (56.25%)were moderately differentiation ,9 patients (28.1%)poorly differentiation and 5 patients (15.6%) were well differentiation. There were no significant differences of radical surgery in elective and emergency presented cases in recurrence and post operative complications.

Key words: Ca. colon, radical resection. Stage 11&111

INTRODUCTION:

In U.S.A carcinoma of large bowel is the second commonest cause of death of malignant disease next to cancer of lung in males and breast in females, may occur at any age, women were affected more than men. ,the sigmoid colon is the commonest site , 5% of the tumors were multiple.^[4]In U.k account for 20000 deaths per year.^[5]Genetically, colorectal cancer represents a complex disease, and genetic alterations are often associated with progression from premalignant lesion (adenoma) to invasive adenocarcinoma, Sequence of molecular and genetic events leading to transformation from adenomatous polyps to overt malignancy has been characterized by Vogelstein and Fearon.^[6]The early event is a mutation of *APC* (adenomatous polyposis gene), which was first discovered in individuals with familial adenomatous polyposis (FAP). The protein encoded by *APC* is important in activation of oncogene *c-myc* and cyclin D1, which drives the progression to malignant phenotype. Although FAP is a rare hereditary syndrome accounting for only about 1% of cases of colon cancer, *APC* mutations are very frequent in sporadic colorectal cancers. In addition to mutations, epigenetic events such as abnormal DNA methylation can also cause silencing of

tumor suppressor genes or activation of

oncogenes, compromising the genetic balance and ultimately leading to malignant transformation. Other important genes in colon carcinogenesis include *KRAS* oncogene, chromosome 18 loss of heterozygosity (LOH) leading to inactivation of *SMAD4 (DPC4)*, and *DCC* (deleted in colon cancer) tumor suppression genes. Chromosome arm 17p deletion and mutations affecting *p53* tumor suppressor gene confer resistance to programmed cell death (apoptosis) and are thought to be late events in colon carcinogenesis^[7]. In 2003, the World Health Organization estimated that approximately 940,000 individuals were be diagnosed with colorectal cancer worldwide and 492,000 died from it that year. Colorectal cancer is a major health burden worldwide. The incidence and mortality from colon cancer has been on a slow decline over the past 20 years in the United States; however, colon cancer remained the third most common cause of cancer-related mortality in 2008^[6]. A multitude of risk factors have been linked to colorectal cancer, including heredity, environmental exposures, and inflammatory syndromes affecting gastrointestinal tract. A review of 8 trials by Rothwell et al found allocation to aspirin reduced death caused by cancer. Individual patient data were available from 7 of the 8 trials. Benefit was

apparent after 5 years of follow-up. The 20-year risk of cancer death was also lower in the aspirin group for all solid cancers. A latent period of 5 years was observed before risk of death was decreased for esophageal, pancreatic, brain, and lung cancers. A more delayed latent period was observed for stomach, colorectal, and prostate cancer. Benefit was only seen for adenocarcinomas in lung and esophageal cancers. The overall effect on 20-year risk of cancer death was greatest for adenocarcinomas.^[8] A study by Burn et al found that 600 mg of aspirin per day for a mean of 25 months reduced cancer incidence after 55.7 months among known carriers of hereditary colorectal cancer; however, further studies are needed to determine the optimum dose and duration of treatment.^[9] Patients with preexisting mental disorders have an overall higher mortality rate than their counterparts. This higher mortality rate can be attributed to a lack of surgery, chemotherapy, and radiation therapy, especially in patients with psychotic disorders and dementia. Improved public health initiatives are needed to improve colon cancer detection and treatment in older adults with mental disorders.^[10] A study by Phipps et al found that smoking is also associated with increased mortality after colorectal cancer diagnosis, especially among patients with colorectal cancer with high microsatellite instability.^[11] A study by Dehal et al found that patients with colorectal cancer and type 2 diabetes mellitus have a higher risk of mortality than those without, most notably a higher risk due to cardiovascular disease.^[12] Recent trends in the United States suggest a disproportionately higher incidence and

death from colon cancer in African Americans than in whites. Hispanic persons have the lowest incidence and mortality from colorectal cancer. A study by Yothers et al found that black patients with resected stage II and stage III colon cancer had worse overall and recurrence-free survival compared with white patients who underwent the same therapy.^[13] A study by Laser et al found that patient navigation increased completion of colorectal cancer screening among ethnically diverse patients. In order to reduce disparities in colorectal cancer screening, targeting patient navigation to black and non-English-speaking patients may be useful.^[14] The incidence of colorectal cancer is about equal for males and females. Age is a well-known risk factor for colorectal cancer, as it is for many other solid tumors. The timeline for progression from early premalignant lesion to malignant cancer ranges from 10-20 years. The incidence of colorectal cancer peaks at about age 65 years. Colorectal cancer is a multifactorial disease process, with etiology transcending genetic factors, environmental exposures (including diet), and inflammatory conditions of digestive tract^[15]. Though much about colorectal cancer genetics remains unknown, current research indicates that genetic factors have the greatest correlation to colorectal cancer. Hereditary mutation of the *APC* gene is the cause of familial adenomatous polyposis (FAP), where affected individuals carry an almost 100% risk of developing colon cancer by age 40 years. Hereditary nonpolyposis colon cancer syndrome (HNPCC, Lynch syndrome) carries about 40% lifetime risk of developing colorectal cancer; individuals with this

syndrome are also at increased risk for urothelial cancer, endometrial cancer, and other less common cancers. Lynch syndrome is characterized by deficient mismatch repair (dMMR) due to inherited mutation in one of the mismatch repair genes, such as *hMLH1*, *hMSH2*, *hMSH6*, *hPMS1*, *hPMS2*, and possibly other undiscovered genes. HNPCC is a cause of about 6% of all colon cancers. Although the use of aspirin may reduce the risk of colorectal neoplasia in some populations, a study by Burn et al found no effect on the incidence of colorectal cancer among carriers of Lynch syndrome with use of aspirin, resistant starch, or both.^[16] Dietary factors are the subject of intense and ongoing investigations.^[17] Epidemiological studies have linked increased risk of colorectal cancer with a diet high in red meat and animal fat, low-fiber diet, and low overall intake of fruits and vegetables. A study by Aune et al found that a high intake of fiber was associated with a reduced risk of colorectal cancer. In particular, cereal fiber and whole grains were found to be effective.^[18] A study by Pala et al found that high yogurt intake was also associated with a decreased risk for colorectal cancer.^[19]

Aim of study:

To evaluate the pattern , incidence of stage 11& 111 of colonic cancer in our city (al nassiryia) and role of radical surgery in emergency presented cases comparing with elective radical surgery in recurrence rate and postoperative complications.

Patients and methods:

This study was done in Al Hussein teaching hospital through 2 years period from April 2008 to March

2010 with follow up for 3 years on 32 patients complaining from stage 11& stage 111 carcinoma of colon clinically and histopathologically diagnosed as stage 11or stage 111 . in order to assess the pattern ,incidence and role of radical surgery in emergency cases and comparing with elective radical surgery in recurrence rate and post operative complications in Al Nassyria city. 10 of those patients are presented as an emergency conditions as acute intestinal obstruction and or uncontrolled bleeding per rectum, while 22 patients presented as an elective cases with signs and symptoms of carcinoma of colon , confirm diagnosis by specific investigations that we mention it above, so after take informed consent from the patients after explain to him (her) why when, who, where and intra and post-operative complications that may occur. we did for those patients mid line incisions, then we went to the site of tumor for recording these information, site of tumor, macroscopical appearance and then resects tumor with about 5 -6 cm from normal appearance of the distal edge with classical malignant resection with ligations and resections of arterial blood supply to that area according to the strategy of resective treatment of carcinoma of colon that we mention it above with the regional lymph node that draining the affected area ,send for histopathology to detect differentiation of tumor and stage classifications, most of elective cases treated with tumor resection and

primary suturing ,while all emergency cases treated with resection and de functioning stoma and then re anastomosis later on. All

patients receive same adjuvant therapy and same preoperative and post operative antibiotics.

RESULTS:

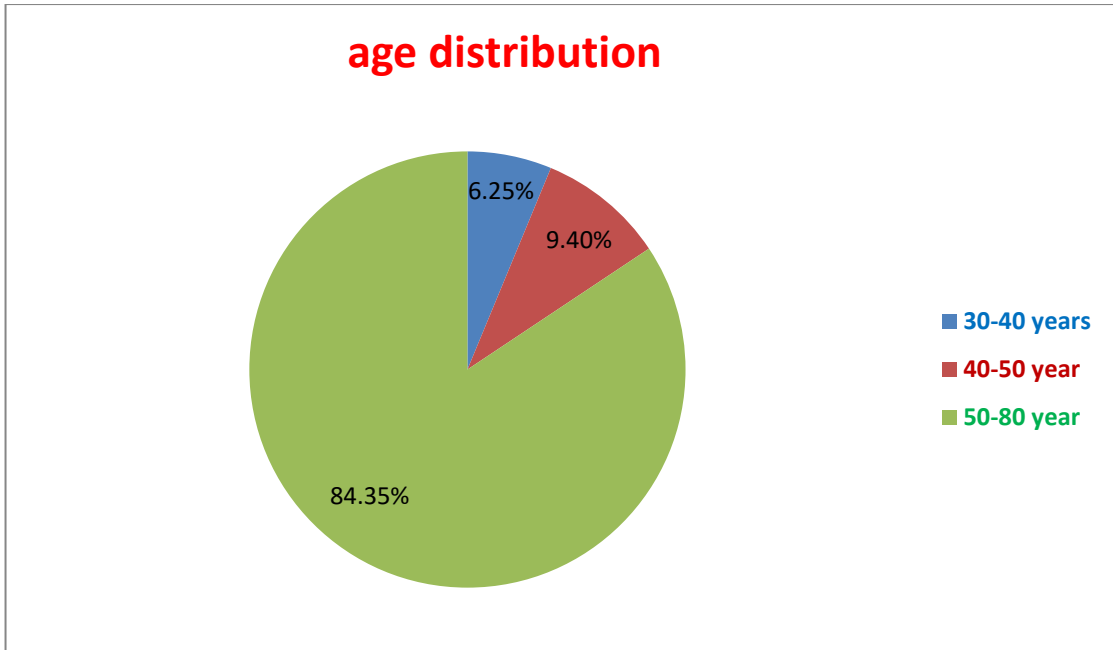
Carcinoma of colon may affect any age but in our study 32 patients who complaining from stage 111 carcinoma of colon . about 84.3% of cases [27 patients] occurred between 50 -80 years, 6.25% of cases[2 patients] at age 30 -40 years and 9.3% (3 cases)at age between 40 -50 years. Males 18patients (56.25%) are more common than female 14 patients (43.73%) ,differ from the U.K and U.S. A. incidence where females affected more than males. About location of tumour; The tumor is more common in the left side involving sigmoid colon in 46.8% of cases [15 patients] , 21.8% [7 patients] involved the right side of colon , and 10 patients (31.3%) have a tumour in transverse and descending colon about macroscopical appearance ,16 patients(50%)were annular type, 12 patients (37.5%) were cauliflower and 4 patients (12.5%) were ulcerative type, about

histopathological study 18 patients (56.25%)were moderately differentiation ,9 patients (28.1%)poorly differentiation and 5 patients (15.6%) were well differentiation. 10 cases (31%) presented as an emergency while 22 caese (69%) presented as an elective cases. There is no significant differences of intra operative and an early post-operative complication after radical surgery in both groups, acute presented cases and elective cases. About recurrent after radical surgery we get 11 patients (34.3%) were have a recurrent within a period between 1.5 to 5 years. 3patients (30%) belong to an acute presented while 8 patients (36.3%) belong to an elective presented cases, 4 of those patients were poorly differentiated group (36.3%) , recurrent period from 1.5 to 2.5 years while 6 patients (54.5%) were belong to moderate differentiated group period of recurrence range from 3 -4 years while well differentiated group 1 (9.2%)patients have recurrent after 5 years from operation .

Elective cases	Emergency cases
22 [68.75%]	10 [31.25%]

DISTRIBUTIONS OF CASES ACCORDING TO PRESENTATION

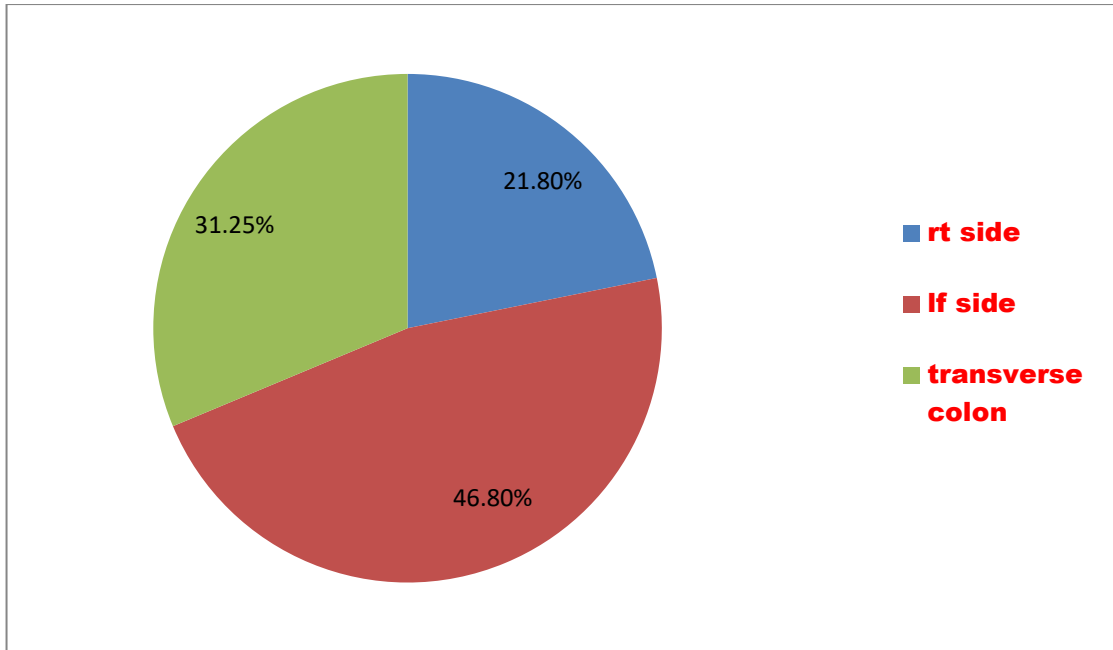
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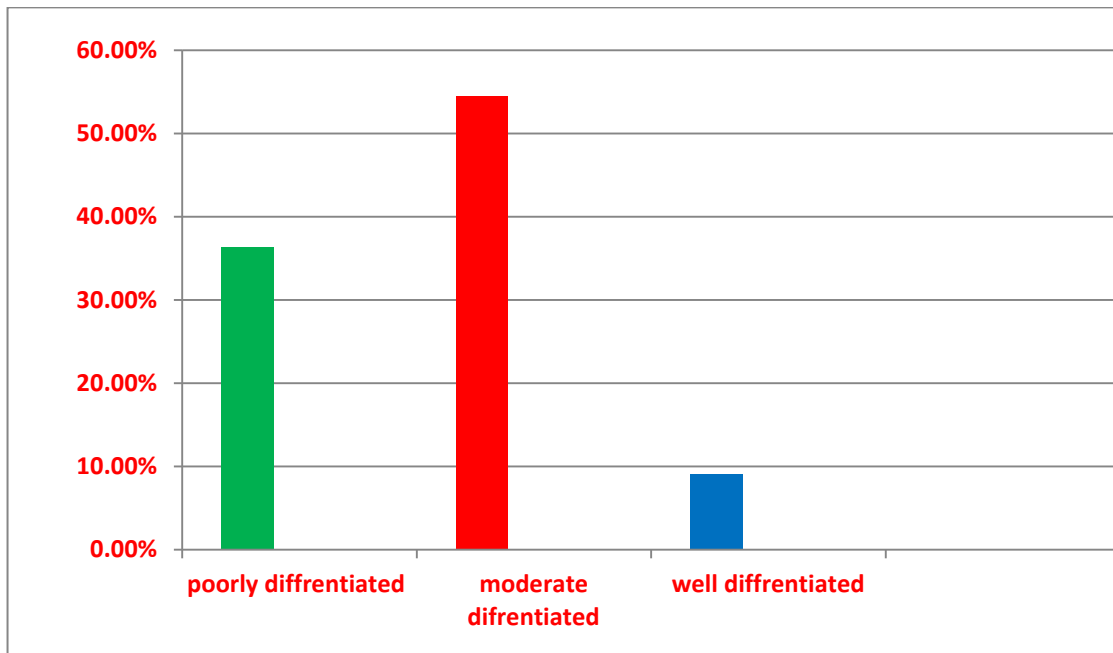


DISTRIBUTION OF CASES ACCORDING TO THE SITE INVOLVEMENT.

TYPES	NO.OF CASES	PERCENTAGE
CAULIFLOWER	12 CASES	37.5%
ANNULAR	16 CASES	50%
ULCERATIVE	4 CASES	12.5%

DISTRIBUTIONS OF CASES ACCORDING TO THE MACROSCOPICAL APPEARANCE

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Percentage of patients who have a recurrent of carcinoma of colon according to differentiations.

Discussion:

Carcinoma of colon is the second common malignant disease affecting male and 3rd common disease affecting female. it's have a different macroscopical appearance (ulcerative, annular, tubular, cauliflower) with different histological grade(well, moderately and poorly differentiated), early detection of this tumor is very important to decrease the morbidity , mortality and improve survival of patients because invasive carcinoma of colon is a preventable disease. so from our study we find there are high recurrent rate even with radical surgery in addition to adjuvant therapy when patients reach to stage 11or stage 111, there are no significant differences between emergency and elective presented cases in doing radical surgery as a

one step . so we prefer to provide our city by specific center for early detection of carcinoma of colon as we mentions above There is no 100%curative surgery in carcinoma of colon , even when patients receive adjuvant therapy post operatively in advance cases. As we see from our study there were a high percentage of recurrence within 5 years of fallow up .

Conclusion:

1-Invasive colonic cancer is a preventable disease when we diagnose the case early , delay in detection of this condition means we will kill the patients even with radical surgery and adjuvant therapy.

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الخلاصة

دراسة طبية اجريت على 32 مريض في مستشفى الحسين بالناصرية يشكو من المرحلة الثانية والثالثة من سرطان القولون لدراسة خاصة ومكان الاصابه بسرطان القولون بمدينه الناصريه وضواحيها وطريقه العلاج الجراحي وخاصة للمرضى اللذين يعانون من الاعراض الحاده لهذا المرض. عشره من هؤلاء المرضى وصلوا الطوارئ وهم يعانون من الاعراض الحاده وهو انسداد الامعاء الحاد وبقية المرضى يعانون من بعض الاعراض والعلامات التي تنطبق على وجود سرطان القولون. تم التأكد من اصابتهم بهذا المرض من خلال بعض الفحوصات المختبريه والكشوف الخاصه مثل الاشعه السينيه والمقطعيه والرنين وناظور القولون وزراعته الانسجه. من خلال هذه الدراسة تبين ان نسبه كبيره منه تصيب الاعمار التي تزداد على 50 سنه بنسبه حوالي 84.3% وقد يصيب هذا المرض أي عمر حتى الاعمار الاقل من 40 سنه لكن بنسبه قليله جدا. وان اصابه الرجال اكثر من اصابه النساء وهذه نسبه مفاجئه لانه عالميا نسبه اصابه النساء اكثر من الرجال اما في دراستنا فان سرطان القولون يصيب الرجال بنسبه 56.25%. وان نسبه اصابه القولون النازل اكثر من اصابه القولون المستعرض او القولون الصاعد بنسبه 46.8% وان معظم المرضى (56.25%) عند تشخيص المرض يكونون قد وصلوا الى مرحله متقدمه منه حيث يكون قد انتشر الى الغدد اللمفاويه المعويه او منتشر الى احد اعضاء البطن الكبد مثلا. اما بالنسبة للعلاج فمعظم الحالات الباردة عولجت باستئصال الورم مع حوالي 5 سم من الجزء السليم المنظور بالعين والربط المباشر للأمعاء مع رفع كل الغدد اللمفاويه وربط الشرايين التي تغذي هذه المنطقه مع رفع المزنتري الملاصق للمنطقه واما بالنسبة للحالات الطارئه فتم رفع الورم مع 5 سم من الجزء السليم المنظور بصريا مع الغدد اللمفاويه والمزنتري مربوط الشرايين المغذيه للمنطقه لكن بدون ربط مباشر حيث تم الربط بعد فتره بين شهر ونصف الى شهرين. معظم الحالات ارسلت لأخذ جرعة من العلاج الكيماوي الإشعاعي بعد العمليه. تبين من الدراسة ان نسبه عوده المرض كبيره تتراوح بنسبه 33% عند تقدم الحاله السرطانية حتى بعد اجراء العمليه الجراحية الشاملة واعطاء المريض الجرعة الكافية من الاشعة او الكيماوي. لذا ننصح بوجود فتح مركز خاص بمحافظة ذي قار يتخصص بالكشف المبكر لسرطان القولون للحد من خطورته.

