

RESEARCH COMMUNICATION

Colorectal Cancer Screening amongst First Degree Relatives of Colon Cancer Cases in Jordan

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Abstract

Objectives: Early detection and screening for colorectal cancer is important among first degree relatives (FDR) of colon cancer cases. **Methods:** Our target population comprised all such FDR, above 40 years of age, registered during the years 2003-2007, Jordan. Detailed information about cancer cases was collected from Jordan Cancer Registry. The screening study was conducted through two stages, where all FDR were examined at their homes for any suggestive related symptoms of colorectal cancer, then those who were suspected to have cancer were referred to hospital for confirmatory colonoscopy. **Results:** First degree relatives amounted to 3,574 subjects, 153 (4.3%) were complaining of signs and/or symptoms suggestive of CRC. Of them 58 (37.9%) did not accept colonoscopy. The confirmation colonoscopy results for the remaining 95 (62.1%) indicated two confirmed CRC cases. Seventy three percent of the suspected cases complained mainly from change in bowel habit and about one fifth felt cramping. **Conclusion:** This study raised the question of cost effectiveness and cost benefits of running a nationwide screening program for such cancer in a developing country. On the other hand it highlights the importance of early detection activities in Jordan as it was the first study to be conducted among a community dwelling high risk population in the country.

Keywords: Colorectal cancer - screening - early detection - first degree relatives - Jordan

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Introduction

Globally colorectal cancer (CRC) is one of the commonest cancers and the third leading cause of cancer death. However, incidence has decreased as a result of effective intervention and life-style changes in the West (American Cancer Society, 2010). About two-thirds of the incident cases occur in developed countries, where colorectal cancer is the third most common cancer in men and second most common in women. It is fourth most common cancer for males and third for females in the Middle East Region, constituting 9.4% of the worldwide rate (Ahmedin Jemal et al., 2007; Al-Madouj et al., 2008; Vir et al., 2010). In Jordan, it ranked the second among all new cancers, and ranked second among males where it affected 203 (11.1%) and second among females, where it affected 168 (9.0%) Tarawneh et al. (2005).

Colon cancer is perhaps the most familial of all common malignancies and inheritance plays a role in the pathogenesis of up to a third of colon cancer cases. Having a family history of colon cancer increases one's risk of developing this malignancy two- to three-fold over the general population risk. Risk is increased further in families with multiple relatives or younger relatives with a colon cancer diagnosis (Solomon et al., 2002; Aronson, 2009). Screening strategies have been developed

to address the familial risk of commonly observed colon cancer. Screening recommendations are empiric and combine the known effectiveness of available screening tools with the observed risks associated with family history.

The goal of screening for colorectal cancer is the detection and removal of adenomatous polyps, which can decrease the incidence of colorectal cancer, and the diagnosis of early stage cancers. Screening reduces mortality both by decreasing incidence and by detecting cancers at earlier, more treatable stages (American college of gastroenterology guidelines for colorectal cancer screening, 2008; American Cancer Society. Screening guidelines. Colorectal cancer early detection) 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 guidelines can cut 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. Screening programs should begin by classifying the individual patient's level of risk based on personal, family and medical history, which together determine the appropriate approach to screening in that person (Fletcher et al., 2003; Winawer, 2005). No screening approaches for

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CRC were adopted in Jordan despite the high prevalence of the disease, the aim of the current work was to screen and early detect the disease among first degree relatives of colorectal cancer patients and to design a prevention and early detection program for colorectal cancers in Jordan.

Materials and Methods

The study was carried out in the Hashemite Kingdom of Jordan in a Ministry of Health hospital (Al-Bashir Hospital which manages more than 85% of cancer cases in Jordan) and the homes of first degree relatives of CRC cases. The investigator obtained an approval to conduct the study from the Ethical Committee of the Jordanian Ministry of Health. Informed consent was obtained from all participants.

Our target population comprised all first degree relatives of all colorectal cancer patients registered during the years 2000-2004. Detailed information about cancer cases was collected from Jordan Cancer Registry for collecting data concerning colorectal cancer patients registered 2000-2004. Data for cancer registration was collected from all possible sources of information in the four health sectors: governmental, military, private, and university. Well-trained designated persons at each institution abstract cancer data from patients' load.

The following techniques were used to fulfill the objectives of the screening revision. 1) The names, addresses and the telephone numbers of colorectal cancer patients during the years 2000-2004 were obtained by an electronic copy from Jordan Cancer Registry. All patients and /or their families that could be contacted were accessed by phone to explain the aim of the study and were informed for possibility of providing free medical advice. They were enquired about the total number of 1st degree relatives, forty years and above, including their age, address details and telephone number.

Home visit appointments for those who accepted to be interviewed were arranged. 2) Sequential (two stage) screening approach was applied where the first stage was conducted through a especially designed questionnaire and referral sheet to collect the concerned data from the first degree relatives of colorectal cancer cases. The data were collected by a team of two doctors and a nurse. The questionnaire included: Personal Data: age, relation degree, gender, residence address, insurance type. Medical history with special emphasis on gastrointestinal suggestive symptoms e.g. stomach ulcers, bowel problems, bleeding, constipation, diarrhea, blood in stool, weight loss, change in bowel movement, cramping pain in lower abdomen, fatigue).

All suspected relatives cases were referred to the nearest hospital for further investigations and confirmatory examination by colonoscopy(second stage). Daily follow up was carried out after medical examination and colonoscopy. Feedback reports from all health sectors regarding suspected relatives were collected. Some suspected relatives refused to be referred to the assigned hospitals for different reasons.

Confirmed cancer cases among relatives were referred to Al-Bashir Hospital for treatment and follow-up.

Results

The total CRC patients registered in JCR during the years 2000-2004, constituted 1782. Those without clear access address constituted 922 (51.7%). The remaining 860 CRC patients' families (48.3%) were contacted to screen for early signs and symptoms of CRC, among their first degree relatives. Only three families out of 860 families did not agree to give details concerning their relatives by phone. Home visits were arranged to all the remaining 857 families (99.7%) for screening the first degree relatives, they amounted to 3574 subjects, 40 years of age and above. The total number of first degree relatives without any CRC signs and/or symptoms amounted 3421 (95.7%). The remaining suspected persons 153(4.3%) were complaining of signs and/or symptoms suggestive of CRC. Of them 58 (37.9%) didn't accept colonoscopy examination for different reasons. The confirmation colonoscopy results for the remaining 95 (62.1%) revealed two confirmed CRC cases. These two cases were referred to Al-Bashir Hospital in Amman for treatment and follow up (Figure 1).

Figure 2 illustrates the use of multiple sequential (two – stage) screening for signs and symptoms of CRC among the first degree relatives, who underwent colonoscopy. Where stage I (signs and symptoms) suggestive of CRC was performed first, and those who screen positive were recalled for stage - II (colonoscopy). The intersection demonstrates the cases that screened positive in both stages.

The age of first degree relatives ranged from 40 to 79 with a mean of 54.1 ± 9.2 years. Males constituted 54.0%

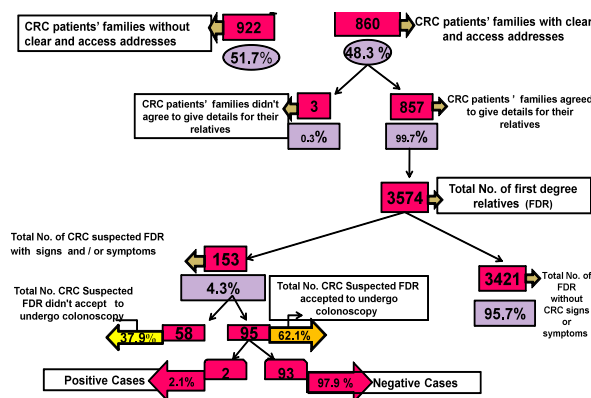


Figure 1. Screening Approach for Relatives of Colon Cancer Cases in the Jordan Cancer Registry

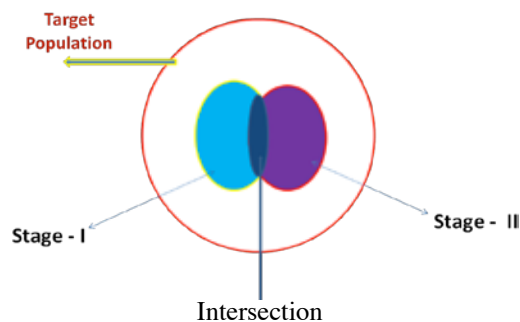


Figure 2. Sequential (Two-stage Screening)

of this population. Nearly sixty percent (59.5%) of the first degree relatives of CRC patients were from Amman governorate, followed by Irbid governorate (19.2%). The total suspected cases were 153 persons, their age ranged from 40 up to 75 years, with a mean of 52.5 ± 7.7 years. The highest percent were in the age group 55 – 59 years (23.5%), one fifth (20.9%) were in the age group 45-49 years, followed by 19.0% in the age group 50 – 54. Males constituted 61.4% of the suspected relatives. More than half of the suspected relatives (59.4%) were residing Amman governorate, followed by Irbid governorate (21.5%).

An interesting finding which was addressed by the current study, that the majority of the FDR didn't know that they are at increased risk of CRC because of this familial relationship, hence they didn't ask for medical advice, counseling and examination for cancer before. It appears from Table 1 that 73.2% of the suspected cases complained mainly from change in bowel habit (i.e. constipation or diarrhea), as the main symptom of colorectal cancer. About one fifth of suspected cases (22.8%) felt cramping, all other signs and symptoms were nearly equally distributed among them.

From the total suspected 153 (4.3%) first degree relatives, only 95 subjects accepted to undergo colonoscopy procedures, of them 2 cases were diagnosed as cancer. Both cases were males, above 50 years of age, complained from changes in the bowel habits and blood in stools. It was poorly differentiated adenocarcinoma, stage II. Table 2 sorts the diagnosis for negative colonoscopy (n=93) from the total (n=95) suspected cases subjected to colonoscopy screening. More than one tenth of the negative results (10.7%) were polyps, while ulcerative colitis and Crohn's disease had the same figure (5.4%). Most were diagnosed with irritable bowel syndrome (43.1%).

Table 1. Distribution of Suspected FDR According to Signs and/or Symptoms, Jordan, 2008

Signs and symptoms	No. (153)	%
Blood in the stool	1	0.7
Weight loss	1	0.7
Change in bowel movement	112	73.2
Fatigue	1	0.7
Cramping + Fatigue	2	1.2
Cramping	35	22.8
Combination of all	1	0.7

Table 2. Distribution of Colonoscopy Screening Negative Diagnoses, Jordan, 2008

Diagnosis	No. (93)	%
Ulcerative colitis	5	5.4
Crohn's disease)	5	5.4
Irritable bowel syndrome	40	43.1
Polyps	10	10.7
Diverticulitis	2	2.2
Coeliac disease	16	17.2
Angiodys plasia	3	3.2
Cytomegalo virus	5	5.4
Dysentery	5	5.4
Ischemic colitis	1	1.0
Pseudomembranus colitis	1	1.0

Discussion

There is a considerable evidence that colorectal cancer screening is both effective and cost effective in reducing the incidence and mortality of this disease. Since 1996 many international groups and policy making organizations have evaluated the evidence on screening, and recommended that all men and women aged 50 and over should be screened for colorectal cancer and adenomatous polyps, and younger in the presence of factors that increase their risk (Pignone et al., 2002)

People who have a first-degree relative who has had colorectal cancer have about twice the risk of developing the disease compared to individuals with no family history (Butterworth et al., 2006; Rubin et al., 2009). About 5%-10% of patients with colorectal cancer have an inherited genetic alteration that causes the cancer. One such disorder is familial adenomatous polyposis (FAP); a second is hereditary nonpolyposis colorectal cancer (HNPCC), also known as Lynch syndrome. Accurate identification of families with a history of colorectal cancer and/or a genetic abnormality that causes colorectal cancer is important so testing can begin at an early age (Cappell ,2005).

Few countries have implemented organized national or regional colorectal cancer screening programs. Many other countries are either pilot testing or considering organized colorectal cancer screening programs (Hawk et al., 2005). The question whether persons at familial or heredity risk differ in terms of absolute, relative or cumulative risk for CRC or not is important for the estimation of the potential of early detection of CRC in a persons with familial and hereditary risks. Therefore, the legal right for screening colonoscopy should be extended to the persons at risk aged 40 to 50 years. Persons suspected for heredity risk should have a genetic counseling and colonoscopy surveillance according to the actual guidelines (Snaebjörnsson et al., 2009). Evidence suggests that CRC screening is a complex behaviour with multiple influences, including personal characteristics, health insurance coverage and physicians' – patient communication (Beydoun et al., 2008).

Families who accepted screening in the present study exceeded 99%. In the U.S. nearly two-thirds of adults are being screened, Joseph DA et al (2002) and colonoscopy is becoming the test of choice. Meissner HI et al (2006). Understanding underlying constructs influencing screening behaviour may improve uptake of CRC screening (Mack et al., 2009) . On the other hand, an epidemiological study of CRC in Iran, mentioned that the rate of colonoscopy screening is very low globally and negligible in Iran and many other developing countries due to cost, resistance by physicians, patients and the health care system (Malekzadeh et al., 2009). These disparities may be related to health care access barriers to CRC endoscopic screening (Hao et al., 2009).

The present study revealed that more than one tenth of the negative colonoscopy results (10.7%) were polyps, while ulcerative colitis and Crohn's disease had the same figure (5.4%). Clearly, it has been well established that patients with chronic inflammatory bowel disease (Crohn's disease and ulcerative colitis) are at greater risk

for developing CR neoplasms. There is also a significant increased risk of developing CRC in patients with ulcerative colitis. In Korea the cumulative incidence of ulcerative colitis (UC) associated CRC was found to be comparable to that of western countries. Hence the follow-up of such cases is of utmost importance (Kim et al., 2009).

In sequential or two-stage screening, a less expensive, less invasive, or less uncomfortable test is generally performed first, and those who screen positive are recalled for further testing with a more expensive, more invasive, or more uncomfortable test, where there is a net loss sensitivity, but a net gain in specificity. It is hoped that bringing back for further testing only those who screen positive will reduce the problem of false positives (Gordis, 2004)

Using sequential (two – stage) screening in the present study yield a net result of 2.1% positive cases. Holliday and Hardcastle (1979) stated that the use of two stage screening tests for early detection of CRC is an effective method. Similar results were drawn from other studies, assuming that detecting cases of disease is more crucial to a screening programme as compared to accurate identification on non- cases, these results suggested that sequential testing has a better diagnostic accuracy than parallel testing (Shirong et al., 2003). It was also reported that the advantage of this combination, lies in its strong negative predictive value, which can decrease the frequency and colonoscopy of follow – up required while those who are positive need more frequent evaluation, added by colonoscopy (Advisory Committee on Cancer Prevention, 1999).

Two prospective studies have evaluated first-degree relatives of individuals with CRC, using colonoscopy. They stated that the majority of relatives had only one FDR with CRC, and FDRs tended to develop adenocarcinoma at an earlier age than controls (Walker, 2007). A case-control study also, revealed that, of the 476 FDRs, only 185(38.9%) agreed to participate in the study and the logistic regression analysis showed that one FDR was a significant risk factor for large adenoma (Fletcher, 2009). However, FDRs of individuals with CRC had a higher incidence of neoplasm (ie, adenomas and carcinomas) compared with individuals with no family history of CRC. The risk was seen to increase with advancing age, whereas colonoscopy appeared to have a detection advantage as a screening tool (Tessaro et al., 2006).

The current study raised the question of cost effectiveness and cost benefits of running a nationwide screening program for colo-rectal cancer in a developing country, on the other hand it highlights the importance of cancer early detection activities in Jordan as it was the first study to be conducted among community dwelling high risk population and how much the knowledge deficiency may significantly affect the screening behavior of high risk population. Upon its results we would build for national community based screening programs in collaboration between MOH and other related sectors to start screening in families with positive history of CRC and polyps at earlier stage and to establish an integrated ongoing public information program to foster a high degree of knowledge amongst targeted population.

Limitations of the study some addresses and telephone numbers of index cases were incomplete or missed. Also some colorectal cancer patients registered in Jordan Cancer registry had died and their families refused to provide any information about their first degree relatives. Cancer phobia, stigma and being a female were the most common reasons for refusal of colonoscopy among the suspected cases.

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