

## RESEARCH COMMUNICATION

# Colorectal Neoplasms in Symptomatic Patients without Evidence of Bleeding: A Prospective Study in an Iranian Population

Yousef Bafandeh\*, Manoochehr Khoshbaten, Amir T Eftekhar-Sadat, Sara Farhang

### Abstract

**Background:** Colorectal cancer (CRC) is a preventable disease with a high mortality and morbidity. Data on its prevalence are lacking in Iran, as well as for adenomatous polyps. This study was conducted to estimate prevalence of CRC in patients with long lasting colonic symptoms (except for known risk factors for cancer and those with rectal bleeding) who underwent total colonoscopy. **Methods:** This prospective study was carried out in Imam Hospital, Tabriz University of Medical Sciences, Iran. The recruitment procedure involved 228 individuals aged more than 30 who visited a gastroenterologist because of lower gastrointestinal tract symptoms and had criteria for a colonoscopy. The endoscopist visualized the caecum in all, documented by a photo of caecum and/or specimen of the terminal ileum. The Chi square test and multiple logistic regression analysis were used to determine the significance of associations between different symptoms and colonoscopic findings. **Results:** Thirty four subjects (14.9%) were found to have colorectal neoplasia and 112 (49.1%) had a completely normal colon. Adenomatous polyps were detected in 27 patients, which included 15.6% of men and 7.0% of women. Most of them were tubular (58.3%) and severe dysplasia was reported in only 3 cases (11.1%). Mean age of patients with a polyp ( $51.1 \pm 12.5$  years) was not significantly different compared to others ( $p=0.381$ ) nor mean duration of symptoms (21.1 months,  $p=0.435$ ). Cancer was detected in 7 (3.1%) of our study population, the mean age of  $65.7 \pm 6.0$  years in this case being significantly elevated ( $p < 0.0005$ ). None of the symptoms were predictors of cancer or polyps. This result was the same by a multivariate analysis including age, gender and duration of the symptoms. **Conclusion:** The low prevalence of colorectal neoplasms as well as the less advanced pattern of adenomas in Iran are compatible with other data from Asia and the Middle East, contrasting with western countries.

**Key Words:** Colorectal cancer - adenomatous polyp - incidence - Iran

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### Introduction

Colorectal cancer as a very common malignancy of industrial countries usually arises from adenomas (Viner et al., 2002). Differences in its mortality have been reported up to 20 fold in different countries (Bond, 2000). Regardless its association with a high mortality, morbidity and cost, it is a preventable disease when early diagnosed (Loren et al., 2002). Epidemiologic studies on different nations and migrated populations strongly support the role of environmental factors as a reason for colorectal cancers such as dietary regimen (Muller and Sonnenberg, 1995).

Autopsy studies have demonstrated high incidence of adenomatous polyps in populations with higher risk of colorectal cancer (Peipins and Sandler, 1994). This rate is reported to be 35-60% in US which has a high incidence of colorectal cancer as well (Correa et al., 1997). These rates are also very similar in European countries (Bombi, 1998).

Asia is known to have a low rate of CRC (Parkin et al., 1997) and has obvious diversity from western countries (Goh et al., 2005). Variety in incidence of colorectal neoplasia is observed in populations and even in cities of one country. Hagigi et al. reported the incidence of colorectal polyps to be 1.6% in an autopsy study in Shiraz, Iran (Haghighi et al., 1997). An increase in incidence of CRC in recent decades has been reported from cancer registry centers in our country (Yazdizadeh et al., 2005). No prospective study was found in a literature review by Medline about endoscopic evaluation of CRC epidemiology in Iran, thus necessitating more evaluation in different populations of the country. Clinical experience of the authors supports a lower incidence of CRC compared with western countries.

Colonoscopic evaluation is usually performed to assess the source of symptoms like changes in bowel habits, abdominal pain or rectal bleeding (Majumdar et al., 1999). Colorectal polyps are asymptomatic most of

\*Corresponding author: Liver and Gastrointestinal Diseases Research Center, Imam Hospital, Tabriz, Iran.  
E-mail: y\_bafandeh@yahoo.com

the time and are discovered in asymptomatic patients undergoing screening; however most of CRC cases are evaluated for clinical symptoms (Rex, 1955).

An earlier prospective study suggested that colorectal symptoms other than bleeding have low diagnostic and differential accuracy for colorectal cancer (Brenna, 1990) with prevalence of lesions being similar in persons with colonic symptoms but no evidence of bleeding and in the asymptomatic population (Rex, 1995). In a study of symptomatic patients (e.g. diarrhea, constipation and abdominal pain; except for rectal bleeding) one malignancy and 17 polyps in 117 patients were found (Yiu et al., 2004). Since colonoscopy is the most precise method in search of a colorectal neoplasia (Hossein et al., 2006) this study intended to estimate prevalence of CRC in a large group of patients with long lasting colonic symptoms (except for known risk factors for cancer like rectal bleeding) underwent the procedure.

## Materials and Methods

This prospective study was carried out in Imam Hospital, Tabriz University of Medical Sciences during May 2005-April 2007. The recruitment procedure involved all individuals aged more than 30 who were visited by a gastroenterologist because of unexplained lower gastrointestinal tract symptoms for more than 3 months and had the criteria for a colonoscopy. Suspected lesions of CRC and polyps were confirmed on histopathological examination of biopsy samples. Total colonoscopy was documented by a photo of caecum and/or specimen of terminal ileum.

Patients with overt GI bleeding (e.g. hematochesia, melena), failure to reach the caecum because of poor preparation or technical problems, those with known polyps referred for polypectomy, a history of previous colorectal neoplasia, unexplained iron deficiency anemia and patients with idiopathic inflammatory bowel disease (IBD) were excluded.

Data analysis was performed using SPSS version 13 software. The Chi square test and Student's t were used to determine the significance of associations between different symptoms and colonoscopic findings. Hazard risk for predictive factors for CRC, including gender, age groups and symptoms, were calculated using multiple logistic regression analysis. A two-tailed test was used for all cases and a P-value of <0.05 was considered significant.

## Results

The study was carried out in 228 consecutive patients undergoing total colonoscopy for lower gastrointestinal symptoms. These patients included 128 men (56.1%) and

100 women (43.9%). Mean age (SD) of the patients was 48.9 (13.41) years. Indications for colonoscopy were as follows: abdominal pain (the most common) in 106 (46.5%), diarrhea in 85 participants (37.3%), constipation in 33 (14.5 %), altering diarrhea and constipation in 17 (7.5%), history of cancer in other organs in 23 (10.1), history of fissure in 3 (0.9%), obstruction in 1 (0.4%), family history of cancer in 9 (3.9%) and screening in 4 (1.8%) patients. Abnormal barium enema was described in 5.3%. Some of the patients had more than one indication for colonoscopy. There was no significant morbidity associated with colonoscopy.

Taking adenoma and carcinoma together, 34 subjects (14.9 per cent) were found to have colorectal neoplasia and 112 (49.1 per cent) had a completely normal colon. Other findings included fistula, angiodysplasia, diverticle, hemorrhoid, fissure, lipoma and non specific erosions or inflammation.

Polyps were detected in 30 participants who included two hyperplastic polyps and as a simultaneous lesion in one patient with CRC. Adenomatous polyp was detected in 27 patients which included 15.6% of men and 7.0% of women ( $p=0.045$ ). Mean age of patients with a polyp was not significantly different compared to others ( $51.1\pm 12.5$  vs.  $48.7\pm 13.5$   $p=NS$ ) neither mean duration of symptoms (21.1 months in patients with polyp vs. 29.40 in patients without). Age distribution of adenomatous polyps and CRC is presented in Table 1. Mean age (SD) of patients with cancer was 65.7 (5.99) years which was significantly more than patients with polyp [ $51.1$  (12.5) years,  $p<0.0005$ ].

Location of the polyps was ascending colon (18.2%), transverse colon (9.1%), descending colon (31.8%), sigmoid (22.7%) and rectum (18.2%). This pattern was almost the same in male and females ( $p=0.231$ ). Most of them were tubular (58.3%) followed by tubulo-villous (25.0%) and villous adenomas (16.7%). Two polyps were serrated adenoma. Severe dysplasia was reported in only 3 cases (11.1%): one tubulo-villous in ascending colon, one tubular polyp in descending colon and one villous polyp in sigmoid. Sizes of polyps are described in table 2. Size of the polyp was not related to age ( $p=0.964$ ,  $r=0.11$ ) or gender ( $p=0.207$ ) of the patients.

Cancer was detected in 7 (3.1%) of our study population which included 3.9% of men and 2.0% of women ( $p=0.471$ ). Mean age of patients with cancer was significantly more than others [ $65.7\pm 5.99$  vs.  $48.4\pm 13.2$   $p<0.0005$ ].

Mean duration of symptoms was not significantly different between two groups (3.0 months in patients with cancer vs. 28.91 in patients without,  $p=0.145$ ). Location of the cancer was caecum (14.3%), ascending colon (42.9%), sigmoid (14.3%) and rectum (28.6%). No difference in age of the patients of right-sided and left-

**Table 1. Colorectal Neoplasms in Symptomatic Individuals Undergoing Total Colonoscopy**

|                    | 30-39<br>(n=76) | 40-49<br>(n=50) | 50-59<br>(n=58) | 60-69<br>(n=25) | 70-79<br>(n=16) | 80<<br>(n=2) | All patients<br>(n = 480) |
|--------------------|-----------------|-----------------|-----------------|-----------------|-----------------|--------------|---------------------------|
| Colorectal cancer  | 0 (0.0)         | 0 (0.0)         | 2 (28.6)        | 3 (42.8)        | 2 (28.6)        | 0 (0.0)      | 7 (3.1)                   |
| Colorectal adenoma | 6 (22.2)        | 6 (25.9)        | 9 (33.3)        | 4 (14.8)        | 1 (3.7)         | 0 (0.0)      | 27 (11.8)                 |

Values in parentheses are percentages

**Table 2. Mean Size (mm) of the Polyps According to Location in Patients Older than 30 Years**

|                  | Mean $\pm$ S.D ( Range)  |
|------------------|--------------------------|
| Rectum           | 13.33 $\pm$ 18.8 (2- 35) |
| Sigmoid          | 17.60 $\pm$ 10.2 (8- 35) |
| Descending Colon | 5.60 $\pm$ 2.50 (2- 8)   |
| Transverse Colon | 5.50 $\pm$ 3.53 (3- 8)   |
| Ascending Colon  | 7.00 $\pm$ 1.41 (5- 8)   |
| Total            | 10.26 $\pm$ 9.59         |

sided cancers or polyps ( $p=0.317$  and  $0.412$ ) or their gender ( $p=1.000$ ) was observed.

Associations between symptoms with endoscopic findings on total colonoscopy were assessed by a logistic regression model. None of the symptoms was a predictor for cancers or polyps. This result was the same even after adding age, gender and duration of the symptoms in analysis.

## Discussion

The rise in incidence of CRC in the Asia Pacific region has been related to the dramatic socio-economic developments (Yiu, 2004). Nevertheless there is a serious lack of epidemiological and clinical data of the disease in Iran. Although this is not a population based epidemiological study, important data about this cancer in a sample of our local population are presented.

CRC incidence by population-based cancer registries shows a wide variability. Geographical and ethnic differences have been observed. CRC as the 4th cancer in Iran has an annual incidence rate of 6 to 7.9 per 100,000. Annual ASR (to world population) is estimated to be 6.7 in males and 5.2 in females in our region (Hosseini et al., 2006) and our country remains a low risk region for this cancer. Conversely; gastric cancer is the most common cancer in our region, with high mortality and morbidity.

In contrast to low incidence of CRC in young-age within western countries (2-8% younger than 40) (Griffin et al., 1991), 15-35% of CRC patients in Middle East and 17% in Iran are under 40 (Ansari et al., 2005). As a consequence we decided to enroll patients over 30 in this study to face a better selection of population at risk.

Colorectal adenoma and CRC were detected in 11.8% and 3.1% of our study population older than 30 and without any known risk factors for CRC. This low rate is compatible with other published data from Asia and Middle East (Wu et al., 2004; Ansari et al., 2005; Hosseini et al., 2006). Life style and western dietary intake with high consumption of red and processed meat have been strongly related to incidence of CRC (Chao et al., 2005; Kesse et al., 2006). Low incidence of colorectal neoplasms in our community may be related to genetic factors or high fiber diet. Westernization of diet and reduction in physical activity of our population make an increase in this incidence expectable in the future.

No gender differences were noted in our patients. The mean age of diagnosis in our cancer patients (in the 6th decade of life) and patients with adenomatous polyp (in the 5th decade) is consistent with established data on the

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disease, which may be a mark of transformation of a polyp to cancer in a 10-year period as well.

There has been much discuss about the anatomic distribution of colorectal tumours. A "left" to "right" sided or proximal shift of tumours has been reported in studies mostly from the USA (Axtell and Chiazzese, 1979; Schub and Steinheber, 1986; Kee et al., 1992; Devesa and Chow, 1993; Obrand and Gordon, 1998; Cucino et al., 2002). Nevertheless, several other studies have shown no such shift (Stewart et al., 1983; Crerand et al., 1991; Sharma et al., 2000; Gomez et al., 2004; Goh et al., 2005). Authors' experience in our region about anatomic sites of adenomatous polyps and CRC (1992 to 2005) showed predominant location of left side (34). In current study majority of polyps (72.7%) were located in the recto-sigmoid region while a shift to right side was prominent in site of CRC. Some previously published studies showed older age of patients with right-sided tumours. No difference in the age of diagnosis of right-sided and left-sided tumours was observed in our patients, in line with one other study (Goh et al., 2005).

The risk of carcinoma developing in colorectal adenomas is influenced by a number of characteristics of both patients and adenomas including age of the patient, size of the adenoma, its villous component and severity of dysplasia (Pikhardt, 2006). Villous adenomas which may become malignant in 29 to 70% over the time, (Wheat and Ackerman, 1971; Welch, 1976) seem to be less common in our community compared to western countries. Size of polyps has been reported as independent predictors of malignancy in colorectal polyps (Nusko et al., 1997; Khatibzadeh et al., 2005). The risk of developing adenocarcinoma is 1% in adenomas of up to 1 cm in size, 10% in adenomas from 1 to 2 cm in diameter and as high as 50% in those greater than 2 cm in diameter (Fenoglio et al., 1977). Regarding the clinical significance of small adenomas, only 4% of adenomas less than 6 mm diameter and 16% of those between 6 and 10 mm are reported to have unfavorable histology (Church, 2004).

More than 58% of observed polyps in our population were tubular and villous adenomas comprised 16.7%. Tubular type adenoma is the most common pattern reported by most of the studies (43, 44). However, in a population based survey report, 53.8% of the polyps were tubulovillous, 36.6% tubular and 8.6% villous adenomas (Husson et al., 2007). Results of the current study shows tubular adenoma as the most common type while its prevalence is higher compared to western articles.

In conclusion; the lower age-matched incidence of colorectal adenoma and cancer in our region compared to western population, smaller size of adenomas, dominance of tubular type and fewer cases with severe dysplasia demonstrates similarity with Asian population in contrast to the West.

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