

RAPID COMMUNICATION

## Clinical predictors of colorectal polyps and carcinoma in a low prevalence region: Results of a colonoscopy based study

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### Abstract

**AIM:** To estimate the prevalence of colorectal cancer (CRC) in patients with long lasting colonic symptoms undergoing total colonoscopy; and to establish clinical features predicting its occurrence.

**METHODS:** This prospective study was carried out in Imam Hospital, Tabriz University of medical sciences, Iran. Continuous patients with long lasting lower gastrointestinal tract symptoms who had the criteria of a colonoscopy were included. The endoscopist visualized the caecum documented by a photo and/or a specimen from terminal ileum.

**RESULTS:** Four hundred and eighty consecutive symptomatic patients [mean age (SD): 42.73 (16.21)] were included. The prevalence of colorectal neoplasia was 15.3% (34 subjects) and 37.7% (181 subjects) had a completely normal colon. Adenomatous polyps were detected in 56 (11.7%) patients, in 12.3% of men and 10.9% of women. The mean age of the patients with a polyp was significantly higher than the others ( $49.53 \pm 14.16$  vs  $41.85 \pm 16.26$ ,  $P = 0.001$ ). Most of the adenomatous polyps were left sided and tubular; only 22.5% of polyps were more than 10 mm. Cancer was detected in 16 (3.6%) of our study population, which was mostly right sided (57.2%). The mean age of patients with cancer was significantly higher than the others ( $60.25 \pm 8.26$  vs  $42.13 \pm 16.08$ ,  $P < 0.005$ ) and higher than patients with polyps [ $60.25$  (8.26) vs  $49.53$  (1.91) ( $P < 0.0005$ )]. None of the symptoms (diarrhea, abdominal pain, rectal bleeding, constipation, altering diarrhea and constipation, history of cancer, known irritable bowel disease, history of polyp and fissure or family history of cancer) were predictors for cancer or polyps, but the age of the patient and unexplained

anemia independently predicted cancer.

**CONCLUSION:** Less advanced patterns and smaller sizes of adenomas in Iran is compatible with other data from Asia and the Middle East, but in contrast to western countries. Prevalence of colonic neoplasia in our community seems to be lower than that in western population. Colonic symptoms are not predictors for polyps or cancer but unexplained anemia and elder age can predict CRC.

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**Key words:** Colorectal cancer; Adenomatous polyp; Colonic symptom; Prevalence; Iran

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### INTRODUCTION

Colorectal cancer (CRC) is a common cancer especially in industrial countries<sup>[1]</sup>. The disease is related to a high mortality, morbidity and cost. It usually arises over several years from adenomas that undergo a series of specific genetic perturbations<sup>[1]</sup> and therefore is a preventable disease when diagnosed early<sup>[2]</sup> and treated.

Epidemiological studies of different nations and migrated populations strongly support the role of environmental factors as a reason for colorectal cancer such as dietary regimen<sup>[3]</sup>. Its incidence is reported to be 35%-60% in US<sup>[4]</sup> which is very close to European countries<sup>[5]</sup>.

It has been considered to be less common among Asians and Caucasians<sup>[6,7]</sup>. However, recent studies have shown an increasing trend in these populations<sup>[8-10]</sup>.

Variation in the incidence of colorectal neoplasia has been observed in populations and even in cities of one country. In 1997 autopsy studies from Iran have reported the incidence of colorectal polyps to be 1.6%<sup>[11]</sup>. Recent

increases in the incidence of CRC have been reported from cancer registry centers in our country as well<sup>[12]</sup>, but there is a lack of published prospective studies about endoscopic evaluation of CRC epidemiology in Iran. Therefore, we felt a genuine need to understand and to define better the characteristics of the in our local population; while our clinical evidence supports lower incidence of CRC compared to western countries.

Screening asymptomatic patients is the most common manner of detecting colorectal polyps in western countries, while most CRC cases are still detected once evaluating clinical symptoms<sup>[13]</sup>. However most asymptomatic people do not accept a colonoscopy yet.

To find out epidemiological variations between Iranians compared with western populations, we carried out a study in symptomatic patients undergoing colonoscopy; investigating whether their symptoms were related to the chance of having a polyp or cancer.

## MATERIALS AND METHODS

This prospective study was carried out in Imam Hospital, Tabriz University of medical sciences, Iran. Four hundred and eighty consecutive participants who visited the same gastroenterologist (17 years experience) because of unexplained lower gastrointestinal tract symptoms for more than 3 mo and underwent total colonoscopy between May 2005 and April 2007 were studied.

The endoscopist visualized the caecum in all subjects, documented by a photo of caecum and/or specimen of terminal ileum. Withdrawal time was 10-20 min. There was no significant morbidity associated with colonoscopy. A few patients were excluded as a result of failure to reach the caecum (because of poor preparation or technical problems) or because they were referred for polypectomy. A biopsy was performed in patients with an infiltrative lesion and/or polyp smaller than 5 mm, while polypectomy was done in polyps more than 1 mm. Polypectomy in 6-9 mm pedunculated polyps and multiple biopsies in sessile ones was achieved. Specimens were then histopathologically evaluated by a pathologist expert in GI disorders.

Data analysis was performed using SPSS version 13 software. The  $\chi^2$  test and student's *t* were used to determine the significance of associations between different symptoms and colonoscopic findings. 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 and a *P*-value of < 0.05 was considered significant.

## RESULTS

The 480 participants included 269 men (56%) and 211 women (44%). Mean age  $\pm$  SD of them was  $42.73 \pm 16.21$ . The indications for colonoscopy are summarized in Table 1.

Taking adenoma and carcinoma together, 72 subjects (15.3%) were found to have colorectal neoplasia confirmed by histopathological examination of biopsy samples and

**Table 1** Long lasting symptoms indicating a total colonoscopy and results regarding each symptom *n* (%)

Indicating symptom	Polyp	Cancer
Rectal bleeding ( <i>n</i> = 142)	20 (14.1)	4 (2.8)
Diarrhea ( <i>n</i> = 164)	7 (4.3)	1 (0.6)
Constipation ( <i>n</i> = 48)	3 (6.3)	2 (4.2)
Altering bowel habit ( <i>n</i> = 27)	1 (3.7)	1 (3.7)
Abdominal pain ( <i>n</i> = 147)	16 (10.9)	7 (4.8)
Irritable bowel disease ( <i>n</i> = 7)	1 (14.3)	0
History of polyp ( <i>n</i> = 4)	0	0
Unexplained anemia ( <i>n</i> = 35)	7 (20.0)	5 (14.3)
Cancer in other organs ( <i>n</i> = 25)	4 (16.0)	2 (8.0)
Family history of cancer ( <i>n</i> = 10)	2 (20.0)	0
Abnormal barium enema ( <i>n</i> = 15)	3 (20.0)	0
Others ( <i>n</i> = 8)	1 (12.5)	1 (12.5)

181 (37.7%) had a completely normal colon. Inflammatory bowel disease was diagnosed in 56 (11.7%), hemorrhoid in 120 (25%), fissure in 14 (2.8%), lipoma in 3 (0.6%), erosion or inflammation in 27 (5.6%). Other findings included fistula, angiodysplasia and diverticle.

During the study we found eight (1.6%) hyperplastic polyps. Four (25%) patients with CRC had synchronous polyps. Adenomatous polyps were detected in 56 patients (11.7%) including 12.3% of men and 10.9% of women (*P* = 0.643); 8 patients (14.3%) had multiple polyps. The mean age of patients with a polyp was significantly higher than that of the others ( $49.53 \pm 14.16$  vs  $41.85 \pm 16.26$  *P* = 0.001). The distribution of adenomatous polyp and cancer according to age trend is described in Table 2. The mean time of symptoms in patients with a polyp (26.58 mo) was not significantly different compared with those without a polyp (27.38 mo).

The mean age of patients and polyp sizes in relation to polyp location are shown in Table 3. The location of the polyps was caecum (4.0%), ascending colon (10.0%), transverse colon (14.0%), descending colon (26.0%), sigmoid (26.0%) and rectum (20.0%). Most of the polyps were tubular (65.0%) followed by tubulo-villous (25.0 %) and villous adenomas (10.0%).

Cancer was detected in 16 (3.6%) which included 3.3% of men and 3.3% of women (*P* = 0.986). The mean age  $\pm$  SD of patients with cancer was significantly higher than that of patients without cancer ( $60.25 \pm 8.26$  vs  $42.13 \pm 16.08$  *P* < 0.005) and that of patients with polyps ( $49.53 \pm 1.91$ , *P* < 0.0005). The mean duration of symptoms was significantly shorter compared with patients without cancer (6.88 mo in patients with cancer vs 27.81 in patients without, *P* < 0.005). The location of the cancer was caecum (14.3%), ascending colon (42.9%), transverse colon (7.1%), sigmoid (14.3%) and rectum (21.4%).

Associations between any of these symptoms and the findings on colonoscopy was assessed by a logistic regression model. Unexplained anemia was an independent predictor for cancer (*P* = 0.004). Unexplained anemia kept its predictive value even after adding age, gender and the duration of the symptoms in the analysis (*P* = 0.006), while age was found as an independent predictor of cancer as well (*P* = 0.037).

Table 2 Age distribution of colorectal neoplasm detected by total colonoscopy in Iranian symptomatic patients *n* (%)

	< 30 ( <i>n</i> = 108)	30-39 ( <i>n</i> = 110)	40-49 ( <i>n</i> = 90)	50-59 ( <i>n</i> = 88)	60-69 ( <i>n</i> = 48)	70-79 ( <i>n</i> = 31)	80 < ( <i>n</i> = 3)	All ( <i>n</i> = 480)
Colorectal cancer	0	0	2 (2.2)	6 (6.8)	4 (8.3)	4 (12.9)	0	16 (3.6)
Colorectal adenomatous polyp	5 (4.6)	10 (9.1)	11 (12.2)	18 (20.5)	7 (14.6)	5 (16.1)	0	56 (11.7)

Values in parentheses are percentages.

Table 3 Age and size of the polyp in the patients according to polyp location (mean  $\pm$  SD)

	Size (mm)	Age (yr)
Rectum	8.83 $\pm$ 13.22	41.80 $\pm$ 13.83
Sigmoid	13.00 $\pm$ 8.48	57.33 $\pm$ 8.43
Descending colon	10.18 $\pm$ 9.08	49.69 $\pm$ 12.10
Transverse colon	5.16 $\pm$ 3.18	41.29 $\pm$ 20.05
Ascending colon	6.60 $\pm$ 1.51	59.20 $\pm$ 8.28
Caecum	8	51.50 $\pm$ 7.77

Patients with diarrhea and constipation had lower chances of having a polyp ( $P < 0.0005$  and  $P = 0.025$  receptively). Diarrhea kept the negative predictive value even after adding age, gender and duration of the symptoms in analysis ( $P = 0.022$ ) while age was found as an independent predictor of polyps ( $P = 0.006$ ).

There was no significant relation between age and location of the polyp or cancer ( $P = 0.606$  and  $P = 0.283$ ). The location of the cancer or the polyp was not related to the gender of the patients either ( $P = 0.336$  and  $P = 0.256$ ).

## DISCUSSION

This report represents the first study to characterize the profile of CRC in symptomatic patients of Iran. Although this is not a population based study, important data about this cancer in a sample of our local population are presented.

The only published report from our province shows age-adjusted rates of CRC (as the 3rd most common GI cancer) to be 6.7 in males and 5.2/100 000 in females in our region<sup>[14]</sup>, which may be influenced by the pathology based manner of the study in part. A report of a recent population based registry from five provinces of Iran showed age-adjusted rates of CRC in Iranian males and females to be 8.2 and 7.0/100 000, respectively while 17% of the cases were younger than 40 years of age at the time of diagnosis<sup>[15]</sup>. This rate decreased to 2%-8% in western countries<sup>[16]</sup>. In contrast to the low risk of CRC in our country, research supports an increase in occurrence of the disease<sup>[17]</sup>. This increase in incidence of CRC in the Asia-Pacific region has been related to the dramatic socio-economic developments<sup>[18]</sup> which can in part explain the higher rate in the younger aged population. The use of fat and thereby prevalence of obesity have increased during the past decade<sup>[19,20]</sup>. Appropriate screening strategies should be considered to decrease the burden of CRC in the young population of Iran. The first step is gathering

satisfactory data on characteristics of the disease to map out an effective plan.

Colorectal adenoma and CRC were detected in 11.7% and 3.6% of our study population with long lasting colonic symptoms. This low rate is compatible with other published data from Asia and Middle East<sup>[15]</sup>. Colonoscopic examination from western countries has shown neoplastic lesions in 37.5% of asymptomatic patients<sup>[21]</sup> which is even higher than our symptomatic (including evidence of bleeding) sample. Genetic factors and the high fibre diets of our community may explain this low incidence but this can be influenced by recent changes like westernization of diet and reduction in physical activity of our population.

No gender differences were noted in our patients. The mean age of diagnosis in our cancer patients and patients with adenomatous polyps (in the 5th decade of life) is consistent with previously established data. Our cancer patients were more than 10 years older than patients with adenomatous polyps which is compatible with transformation of a polyp to cancer in a 10-year period. The incidence of colorectal cancer increases with age. Risk of colorectal cancer increases slightly after the age of 40 and more sharply after 50 years<sup>[22]</sup>. This pattern was also observed in our study. Older age is an independent predictor for polyp and cancer in our population. Lower gastrointestinal symptoms are not predictive of colorectal neoplasia in our study as supported by reports from western countries<sup>[23]</sup>. This may be explained simply by the frequency of lower gastrointestinal symptoms in the general population. However, the rate of rectal bleeding in this study is considerably higher than that in the general population, while a possible explanation is that there is a high prevalence of benign disease likely to cause rectal bleeding. Unexplained anemia is the only sign which can predict CRC.

The characteristics of both patients and adenomas can influence the risk of carcinoma developing in colorectal adenomas. These are the age of the patient, size of the adenoma, its villous component and the severity of dysplasia<sup>[24]</sup>. Villous adenomas seem to be less common in our community compared with western countries, which may become malignant in 29% to 70% of the time<sup>[25-27]</sup>. The majority of polyps detected in our study population were tubular (65%) and villous adenomas comprised 10%.

The size of polyps has been reported as an independent predictor of malignancy in colorectal polyps<sup>[28,29]</sup>. The risk of developing adenocarcinoma is 1% in adenomas of up to 1 cm in size, 10% in adenomas from 1 cm to 2 cm in diameter and 50% in those greater than 2 cm in diameter<sup>[30]</sup>. Only 4% of adenomas less than 6 mm diameter, and 16% of those between 6 mm and 10 mm are reported to have

unfavorable histology<sup>[31]</sup>. According to our results, 40.0% of polyps were less than 6 mm, 37.5% were between 6-10 mm and 22.5% were more than 10 mm which shows smaller groups at higher risk of malignancy.

There has been much discussion about the anatomical distribution of colorectal tumours. A “left” to “right” sided or proximal shift of tumours has been reported in studies mostly from western countries<sup>[32-35]</sup>. Nevertheless, several other studies especially from Asia have shown no such shift<sup>[36-42]</sup>. In the authors’ experience in our region about anatomic sites of adenomatous polyps and CRC (1992 to 2005), there is a predominant location of left side<sup>[43]</sup>. The study was based on evaluation by colonoscopy and barium enema in patients with colorectal adenoma or CRC. In the current study which is based on findings of total colonoscopy, more than 40% of polyps were located in the recto-sigmoid region while a shift to the right side was prominent in the sites of CRC. The former retrospective study focused on patients with adenomatous polyp or CRC among patients evaluated by colonoscopy. Based on this study with a large number of cases, an anatomical distribution pattern and left shift of colorectal adenomas and cancer is compatible with data from most Asian countries. However, the current study was designed on patients with different lower GI symptoms evaluated for colorectal neoplasms. The right side dominance of CRC in this study is more likely not due to a true increase in right-sided tumors but may be a result of a small number of recorded cancer patients as well as younger ages in our study population.

Some previous published studies showed older ages 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 which has been noted in other studies as well<sup>[7]</sup>.

Although most cases of rectal bleeding were due to self limiting diseases in our study, the probability of colorectal cancer increases significantly both in people older than 60 years and in association with unexplained anemia indicating the need for a more thorough investigation in such cases.

Smaller size of adenomas, dominance of tubular type and fewer cases with severe dysplasia among colorectal adenoma and lower incidence of cancer in our region compared with western populations is comparable with Asian populations and may suggest that it is not a serious health problem of our community at present. Although suspicious symptoms clearly call for urgent investigation, it is important to recognize lower gastrointestinal symptoms are not predictive of cancer except for unexplained anemia in elderly patients.

## COMMENTS

### Background

Colorectal cancer (CRC) is a common cancer especially in industrial countries and is a preventable disease when diagnosed and treated early.

### Research frontiers

Screening asymptomatic patients is the most common way of detecting colorectal polyps while most cancer cases are still detected once evaluating clinical

symptoms. However most asymptomatic people do not accept endoscopy yet. We carried out a study in symptomatic patients undergoing colonoscopy; investigating whether their symptoms were related to chance of having a polyp or cancer.

### Related publications

Colonoscopic examination from western countries has shown neoplastic lesions in 37.5% of asymptomatic patients which is even higher than our symptomatic. An increase in the incidence of CRC in the Asia-Pacific region is noted and has been related to the dramatic socio-economic developments.

### Innovations and breakthroughs

This report represents the first study to characterize the profile of CRC in symptomatic patients of Iran. Although this is not a population based study, important data about this cancer in a sample of our local population are presented.

### Applications

Colonic symptoms are not a predictor for polyp or cancer but unexplained anemia and older age can predict CRC. Less advanced patterns and smaller sizes of adenomas in Iran is compatible with other data from Asia and Middle East, in contrast to western countries. The prevalence of colonic neoplasia in our community seems to be lower than that in western populations.

### Terminology

Colorectal polyps arise from normal epithelium of the colon after some abnormal changes in genes and may develop to colorectal cancer over time.

### Peer review

This is a potentially interesting manuscript, which describes a prospective colonoscopy based study investigating the prevalence of colorectal polyps and cancer in patients with persistent (> 3 mo) colonic symptoms with the aim of determining whether or not the indications were predictive for the presence of either polyp or CRC. The study group was large (480 patients), indications for colonoscopy diverse and the average age profile relatively young (about 43 years). The results section was rather disjointed and could have been better presented and aided by additional tables and figures.

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