Participation Rate and Results of Screening Colonoscopy in Egyptians with Family History of Colorectal Cancer

Ahmed Elwassief[1], Ali Ibrahim Soliman, Badr El-Deen Hemeda Mostafa[2], and Emadeldin R Matar[3]

[1]Internal medicine Department, Gastroenterology Unit. Alhossien Hospital. Alazhar University, Cairo, Egypt
[2]Tropical Medicine Department. Alhossien Hospital. Alazhar University, Cairo, Egypt
[3]Pathology Department. Alhossien Hospital. Alazhar University, Cairo, Egypt
ahmedelwassief@gmail.com

Abstract: Introduction: Colorectal cancer "CRC" is a disease with known risk factors. Family history of CRC is one of the well established risk factors for the disease. CRC has a variable incidence worldwide and the presumable low incidence in Egypt did not rationalize for the development of screening program up till now. **Aim of the study:** The aim of this study is to screen for CRC in patients with intermediate risk "those with family history" using colonoscopy. **Results:** In this study 37.3 % of the interviewed population agreed to participate in the study. Among them CRC was found in 2 out of 547 patients 0.4%. Both patients were males above 60 years old. Abnormalities were mapped in relation to age and showed that age groups [40-50] and above 60 had the highest rate of advanced adenoma 4.6% and 4.5% respectively. No relation was found between the development of adenoma and the number of family members with CRC or history of smoking. **Conclusion:** Egypt has a low incidence of CRC in individuals with family history of CRC. The percentage of younger population with advanced adenoma should be interpreted cautiously in view of the high participation rate of this age group in the study representing 40% of the total sample.
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1.Introduction:

Colorectal cancer is one of the three most common cancers in developed countries and is one of the three most common causes of cancer related death in industrialized countries **(1).** The data about the prevalence of CRC in Egypt are lacking. In one study CRC represented only a proportion of 4.4% of newly diagnosed cancer compared to 13 % in western countries **(2).** However, another study concluded that CRC is not uncommon in Egypt and represented 10.6% of cases with symptomatic colonic disease's **(3).** This lack of evidence might be attributed to the lack of effective cancer reporting and surveillance system in Egypt. Up till now the recognized low incidence of CRC in Egypt did not justify the launch of a screening program for this disease. CRC can effectively be prevented if adenomatous polyps are diagnosed early using a screening program **(4).** FOBT, barium enema, and screening colonoscopy were all used as screening tools. However, effective screening faces many barriers. The coast of the procedure, social, cultural factors, and lack of symptoms might all be causes for refusal of participation in CRC screening especially colonoscopy. Up to 20% of patients with colorectal cancer have a first degree relative with CRC, and it is estimated that having a first degree relative with CRC nearly doubles the risk of developing CRC **(5).** Current guidelines state that patients with family history of CRC should start their screening for CRC by the age of 40 or 10 years younger than the earliest diagnosis in their families **(6).** Commercially available FOBT that is used at present is an unrehydrated guaiac test (GT) has a sensitivity of (24%) for detecting advanced colonic neoplasms **(7)** and positive predictive value of 10% for CRC **(8).** This stumpy degree of sensitivity gives colonoscopy its priority as an ideal tool for early detection of colon adenomas and colorectal cancer. So we started a screening program in our hospital targeting individuals at high risk of developing CRC.

Aim of the study:

The aim of the study is to determine the prevalence of CRC and advanced adenomas in high risk individuals "those with family history of CRC".

Study design:

Cross sectional study.

2. Patients and methods:

High risk individuals were identified using a questionnaire of patients referred to the gastroenterology outpatient clinic of Alhussien University hospital in the period between 1st of January 2007 till 1st of January 2012. The hospital is located in the city of Cairo and receives its catchments population of about 80% of urban population and about 20% from rural areas or villagers. All patients undergoing visits were

questioned about family history of cancer colon. Identified subjects were offered detailed description about the risk of CRC and the exact protocol of the study, and were invited in a straight line to do colonoscopy. All patients had at least one 1st degree relative with colorectal cancer. Patients' basic demographic data including age and gender were recorded. Additionally, the number of family members with history of CRC, history of alcoholism, tobacco smocking and NSAID treatment were all documented. Patients with suboptimal preparation or incomplete examinations were excluded from final analysis of data.

Colonoscopy procedure:

Colonoscopy was done under conscious sedation using "2.5-7.5 mg midazolam" using Olympus colonoscope (CFQ240AL, *Olympus* Optical Co Ltd., Tokyo, Japan). Details of the lesions as site, size and morphology were all documented. Lesions were divided according to size into less than or equal to 1 cm and more than 1 cm. Morphology of the lesion "Flat, ulcerative, polyploid or mixed polypoid/ ulcerative lesion" was recorded. The location of the lesion was documented as either Proximal (caecum, ascending colon, hepatic flexure and transverse colon) or distal (splenic flexure, descending colon, sigmoid colon and rectum). Histological classification was reported as cancer, advanced lesions "adenomatous polyps with high grade dysplasia, larger than one centimeter or with significant villous component (>25%)" **(9),** and non advanced lesions "adenomatous polyps with low grade dysplasia, hyperplastic polyps, bilharzial polyps or inflammatory polyps".

Statistical analysis:

The analysis was performed using statistical software package (SPSS 17.0 version for Windows; SPSS Inc., Chicago, IL, USA). Descriptive statistics were recorded as percentage % in relation to total number. Student t-test "results were recorded as mean and standard deviation" was used to compare the mean values of continuous variables. The Chi-square $\chi 2$ test was used for the analysis of categorical data in detecting statistically significant differences between different groups. P values below 0.05 were considered statistically significant. All values were presented as the mean ± standard deviation unless mentioned otherwise.

3.Results:

Within the period from 1-1-2007 till 1-1-2012, target subjects were identified using a questionnaire of patients referred to the gastroenterology outpatient clinic. 1470 subjects were identified. Identified subjects were offered detailed description about the risk of CRC and the exact protocol of the study and 653 agreed to participate in the study. 96 patients were either lost or refused to do colonoscopy after initial evaluation. Additional 10 patients were excluded because of incomplete colonoscopy. Finally 547 were eligible for this study; out of them 61.4% were males. Mean age of screened population was 49±9. Sixty nine patients 12.6% had abnormal colonoscopy. The observed abnormalities were as following "0.4% of subjects had adenocarcinoma, 3.5 % had advanced adenoma, 4.9 % benign adenoma, 1.8% inflammatory lesion, 1.6 % hyperplastic polyp, and 0.4 % had bilharzial polyp" (Table 1).

Table 1; Epidemiology of the screened population:

Factor	Mean or %
Rate of colonoscopy acceptance	37.3%
Gender acceptance rate	
Male	336/751=44.7%
Female	211/719 = 29.3%
Age	49 ± 9
Sex	
• Male	(336) 61.4
• Female	(211) 38.6
Lesions Total	**(69) 12.6**
• Hyper-plastic polyps	(9) 1.6
• Non-specific inflammatory lesions	(10) 1.8
• Bilharzial polyp	(2) 0.4
• Benign adenoma	(27) 4.9
• Advanced adenoma	(19) 3.5
• Carcinoma	(2) 0.4

Nearly 40% of the participants were in age group (40-50 years old).The age group distribution of abnormal colonoscopy showed that subjects above 60 years old had the highest prevalence of abnormalities (18.2%), followed by individuals between 40-50 year old (13%), next were patients between 50-60 year old (12.3 %), and lastly patients less than 40 year old (7.2%) (Table 2). On the other hand advanced adenomas were more prevalent in patients between 40-50 year old (4.6%) followed by patients above 60 year old (4.5%). Patients between 50-60 year old and patient below 40 years old had the same prevalence of advanced adenoma. (Table 2)

Advanced adenomas were more frequent in distal than proximal colon 68.4% versus 31.6%. Mean age didn't significantly differ between both groups. Mean size of advanced adenoma was 17.3 mm versus 4.2 mm for benign lesions [P =.000] (Table 3).

2 cases of adenocarcinoma were reported 0. 4% and they were both in patients over 60 year old [P=.019], they were both males, and both lesions

were distal AND sized >1cm [P =.03]. In regards gross morphology, 33.3% of mixed lesions were malignant versus 1.9 % of polypoid and 0% of both flat and pure ulcerative lesions [P =.046]. Neither history of significant smoking, nor the number of family members with history of CRC was related to CRC detection (Table 4).

Table 2; Age distribution of lesions

Factor		% of total lesions	Total	% within groups
Age distribution of all lesions	**All ages**	**100.0%**	**69/547**	**12.6%**
	<40	17.7%	7/97	**7.2%**
	40-50	39.5%	28/216	**13 %**
	50-60	26.7%	18/146	**12.3%**
	>60	16.1%	16/88	**18.2%**
Age distribution of advanced adenoma	**All ages**	**100.0%**	**19/547**	**3.5 %**
	<40	17.7%	2/97	**2.1%**
	40-50	39.5%	10/216	**4.6%**
	50-60	26.7%	3/146	**2.1%**
	>60	16.1%	4/88	**4.5%**

Table 3; characteristics of advanced adenomas:

Factor	Lesion/Total	% or Mean + SD	p
location			
• Proximal	6/19	31.6%	
• Distal	13/19	68.4%	**ns**
Age			
• Advanced Adenoma	19	**50** ± **9**	
• Non advanced	528	**49±9**	**ns**
Size			
• Advanced Adenoma	19	**17.3±9**	**0.000**
• Benign lesions	47	**4.1±8**	

Table 4; characteristics of CRC lesions:

Factor	Number	Mean + SD	P
Age groups			
• <40	0/97	0%	
• 40-50	0/216	0%	
• 50-60	0/146	0%	**.019**
• >60	2/88	2.3%	
Sex			
Male	2/336	.6%	**ns**
Female	0/211	0%	
Location of cancer			
• Distal	2/46	2.9%	**ns**
• proximal	0/23	0%	
Morphology			
Polyploidy	1/54	1.9%	
Ulcerative	0/4	0%	
Mixed "ulcerative"	1/3	33.3%	**.015**
flat	0/8	0%	
Size			
<1cm	0/48	0%	**.03**
>1cm	2/21	9.5%	
Family members			
one	2/535	0.4%	**ns**
more	0/12	0%	
Smoking			
Yes	2/467	0.4%	**ns**
No	0/60	0%	

4. Discussion:

CRC is the result of interaction between genetic predisposition and environmental factors as "life-style, smoking, and dietary factors". The adenoma carcinoma progression theory that takes about 10 years to occur is considered the cause of most CRC cases **(10).** Colonoscopy is considered to be the gold standard for early detection of colon adenomas and colorectal cancer. Screening colonoscopy can prevent CRC by detection and removal of adenomatous polyps, or it can significantly improve patients' survival if CRC is diagnosed while in early stages **(4).** Irrespective to age, patients with one first-degree relative has a 2-fold higher risk of CRC while patients with two or more relatives have a 4-fold increased risk **(11).** Current guidelines recommend that individuals with first degree member family history of CRC should have screening procedures at age 40 years or 10 years younger than the earliest diagnosis in their family **(6).**The incidence rate of cancer colon in Egypt was reported to be 2.7 while that of cancer rectum was 1.7 **(2).** In one study 38% of Egyptian patients with CRC were younger than 40 year old **(12).** Although, incidence rate of CRC in Egypt is low, but it is presumed that environmental factors as pesticides can cause regional variation in incidence rate as Egyptian farmers diagnosed with colorectal cancer were proved to have high serum organochlorines **(13).** The low incidence rate of CRC was a barrier against the implementation of a screening program, and to our knowledge no previous studies had aimed to screen CRC in Egyptians. The aim of the study was to evaluate the results of screening colonoscopy in patients with family history of CRC and to map the age specific incidence of abnormalities in colonoscopy in Egyptian populations.

37.3% of the initially evaluated individuals agreed to participate in this study and complied to do colonoscopy which is considered higher than reported by *Lisi et al., 2010,* who reported 10% compliance rate **(14).** However all their patients were average risk and not intermediate risk as our sample individuals. The acceptance for colonoscopy was higher among males than females 44.7% versus 29.3%. Eventually 61.4% of the participants were males which might reflect a social and cultural barrier [Table 1]. Other studies pointed that female are less likely to approve on undergoing sigmidoscopy because of social factors **(15).** It is established that many factors affect the decision of accepting an invitation for colonoscopy. Economic, social, and circumstantial factors can influence the decision, as if it was done upon personal interview or by the phone and the degree of effective delivery of information and risk stratification of the patient **(16).** Previous studies proved that fear of the test itself (colonoscopy), fear of cancer diagnosis, fear of burdening family members, violation (among men) and embarrassment (among women) were also barriers for participation in colonoscopy screening program **(17).** Fatalism and health literacy were also contributing factors in refusal of CRC screening in some ethnic groups **(18).**

Abnormalities were noticed in 12.6% of individuals [Table 1]. Most of the abnormalities were found in the age group [> 60 years] with a prevalence of 18.2%, while least of the abnormalities were reported in those < 40 years 7.2% [Table 2]. Adenomatous polyps were found in 8.4% of screened persons and advanced adenoma was found in 3.5% of individuals [Table 1]. Age specific distribution of advanced adenoma revealed that patients between {40-50 years old} had the highest rate of adenoma detection 4.6%. The rate was almost similar to those above 60 years old 4.5%. This similarity might be due to selection bias with large number of patients in the {40-50 years old} age group "almost 40% of all studied population versus 16% in the persons above 60 years old, consequently their results might had been more representative of the extent of the problem. In another way patients above 60 years old and due to the relative small number might not reflect the true rate of advanced adenomas in their age group. On the other hand many reports had pointed that the incidence of CRC in Egypt is high in younger persons. In one study 38% of Egyptian patients with CRC were younger than 40 year old (12). This conclusion was confirmed later by other investigators **(19).** Another research group concluded that patients with CRC had the youngest mean age among reported gastrointestinal neoplasms in Egypt (44.11 +/- 14.08 years) and that the incidence of CRC had rose in patients between 40-60 years compared to other age groups within the preceding decade of the study **(20).** Putting this with the report that 78.6% of CRC cases in Egypt develop on top of adenomatous polyp **(21)**. And in view of the classically documented progression rate of adenoma to carcinoma that usually develop within the range of 5-10 years as the risk of progression escalate from 4% to 7.4% respectively **(10)** & **(22)**, so a parallel high rate of adenomas can be expected within the age groups between (30-50 years) among Egyptians. In one Egyptian study the rate of adenomatous polyps was 7% in colonoscopies of symptomatic patients but the authors didn't specify the exact rate of advanced adenomas **(23)**. In another study the rate of adenomatous polyps was 3.7% but more than 63% of the participants were either children or teens (24).We observed that advanced adenomas were more in the distal colon 68.4% [Table 3]. This distribution is similar to that reported in ***Zaher et al 2007*** **(24)**.

In our study CRC was found 0.4% of screened individuals "two patients". In one Spanish study CRC was found in 1.9% of 1st degree relatives of CRC patients, however in that study 14.8% of the participants had criteria of lynch syndrome which was not fulfilled in any of our screened individuals **(25)**. In another French study the rate of carcinoma in relatives of patients with large adenoma was reported to be 4.2% and the rate was higher in patients with family history of large adenoma and were younger than 60 years old **(26)**. In one Iranian study CRC was detected in 2.2% of relatives of CRC patients **(27)**. This variation in rate of detection might reflect epidemiological and methodological differences between these studies, however it still support the notion the incidence of CRC is low in Egypt. Age-Standardized Incidence Rates of cancer colon and rectum in Egypt is among the least reported ones World wide. The reported Incidence Rate of cancer colon and rectum in Egyptian males was (4.6 and 2.3 respectively*)* versus (7.6 and 3.9) for Jordan, (11.5 and 9) for china, (14.5 and 11.7) for Poland, and (25.9 and 13) for whitish Americans. While the incidence rates in Egyptian female was reported to be (3.3 and 1.8), versus (7.2 and 4.0) for Jordan, (12.0 and 7.5) for china, (10.4 and 6.9) for Poland, and (19.6 and 8.2) for white USA **(2).** Both of CRC diagnosed patients were males and lesions were distal. They were both above 60 year old [P =.019] [Table 4].Age specific incidence of cancer colon in males showed a progressive rising in incidence reaching maximum in patients over 70 **(2).** Both lesions had a polypoid proportion [P =.015] this is on line with *Kaku et al., 2011* who reported that most CRCs had polypoid lesions **(28)**. The observation that smoking was not a significant risk of CRC should be interpreted cautiously as the number of smokers in the sample was only 60 person "less than 10% of the sample size". Also the lack of association between the number of family members with history of CRC and the occurrence of CRC should be observed with caution as only 12 persons had more than one family member with CRC. We are aware that lack of control group of individuals with average risk is a limitation of this study, but recruiting individuals with average risk for screening colonoscopy was difficult in view of the reported low incidence in Egypt, Health literacy and fatalism.

Conclusion:

We conclude that Egypt is a country with low-risk of CRC that affects mainly older individuals. The high rate of young patients with advanced adenomas needs to be verified carefully taking in consideration the percentage of younger generation among the entire population compared to the developed world.

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