



Relationship of Colorectal Polyps Emergence with Age and Polyp Histopathology

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ABSTRACT

Aims Two-thirds of all colonic polyps are adenomas, which are dysplastic and have the potential for malignant transformation. This study aimed to assess the prevalence of colorectal polyps and its relation with patients' age and polyp histopathology.

Instrument & Methods This cross-sectional retrospective study was conducted on patients attending Gastroenterology and Hepatology Teaching Hospital, a major tertiary hospital in Iraq, who underwent colonoscopy for various indications from January 2020 to April 2022 using a colonoscopic and histopathologic reporting database. The eligible number of patients was 3494. Age, sex, symptoms, indications for colonoscopy, polyp types, location, size, histopathologic types, and grading of dysplasia were collected by manually reviewing the files. The chi-square test was used for categorical data.

Findings The polyp detection rate was 16.3%, increasing with age reaching (46.7%) at age ≥ 60 . The adenoma detection rate was 5.8%, with the highest (18.7%) at age ≥ 60 , with no difference between males and females. Retention and inflammatory polyps are the commonest findings in patients < 30 years old, while most patients with adenoma were ≥ 30 years old. Younger patients tended to have more distally located lesions compared with older patients with lesions at different levels; high-grade dysplastic adenoma had more pedunculated morphology (38.6%) and their size ≥ 1 cm in 63% of patients.

Conclusion Increasing age is associated with an increased prevalence of colorectal polyps, especially adenoma, with male predominance. Tubulovillous adenoma and adenoma with advanced pathology are common findings. Over 1cm pedunculated polyps are associated with high-grade dysplasia.

Keywords Adenoma; Colorectal Carcinoma; Polyp; Prevalence

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Introduction

Colorectal carcinoma (CRC) is the second-leading cause of cancer-related death in the Western world. It accounts for 8% of all cancer deaths worldwide and is the second most common disease in women and men [1]. Asia and Eastern Europe have experienced the greatest increases in colon cancer incidence [1, 2]. Because more precursor lesions are being detected and removed promptly by colonoscopies, recent cancer data show a declining trend in the incidence of colorectal cancer in the United States [3].

It is well established that adenomas, via the adenoma-carcinoma sequence, are the source of 60-90% of this cancer. Most of the time, this transition happens slowly and can take up to 10-15 years. Endoscopic polyp removal can prevent CRC because of this delayed growth [4]. The adenoma-carcinoma sequence may not be the only mechanism of carcinogenesis in older individuals; Polyps emerging at advanced ages may also have a higher intrinsic propensity for malignant transformation, needing less time for cancer to develop from benign adenomas [5-7]. Because colonic polyps, particularly adenomatous ones, are a risk factor for CRC, they are considered significant [8].

Colonic polyps can be classified into two major groups: Neoplastic (adenomas and carcinomas) and non-neoplastic. Neoplastic polyps can cause ulceration and bleeding, while large polyps rarely obstruct the intestine. A polyp propelled downstream by a peristaltic wave can stretch its blood supply and nerve fibers, resulting in abdominal pain [4]. Screening programs have demonstrated efficacy in reducing the incidence and mortality of CRC, one of the few diseases for which this is true [1]. Repetitive fecal occult blood testing (FOBT) has been shown in randomized controlled studies to reduce CRC mortality by 16%, whereas flexible sigmoidoscopy reduces CRC incidence and mortality by 18% and 28%, respectively. It remains to be established in a randomized study whether full colonoscopy, as opposed to flexible sigmoidoscopy, has a greater potential influence on decreasing the incidence and mortality from colorectal cancer [9]. Colonoscopic polypectomy reduces cancer incidence by 76-90% compared to a general population registry, according to multiple cohort studies and randomized clinical trials [10].

One of the most often carried out medical procedures in the United States is the colonoscopy, which serves as the primary screening test or the follow-up method for all screening strategies [11, 12]. The most frequent neoplasm seen on screening colonoscopies and in diagnostic colonoscopies performed on symptomatic people over 50 is colorectal adenomas. Regarding the likelihood that an adenomatous polyp may proceed to cancer, these lesions can be categorized as low-, moderate, or high-risk [13]. It is deemed advanced when a lesion is larger than 1cm,

has a villous component, or has high-grade dysplasia. The occurrence of adenomas and dysplasia is thought to be associated with age, and its frequency rises after reaching the sixth decade of life [14].

This study aimed to estimate the prevalence of colorectal polyps and adenomas and evaluate its relation to patients' age and polyp histopathology.

Instrument and Materials

This cross-sectional retrospective study was conducted on patients attending Gastroenterology and Hepatology Teaching Hospital, a major tertiary hospital in Iraq (Medical City, Baghdad), who underwent colonoscopy for various indications from January 2020 to April 2022 using a colonoscopic and histopathologic reporting database. G*power statistical software was used in this study to calculate the sample size. All patients underwent colonoscopy for various indications, whose described evidence of polyp/s in their reports was considered for analysis. Those records that had incomplete procedures or were assigned by an endoscopist for re-examination for any reason, as well as those negative for the polyp, were excluded.

The data, including age, sex, symptoms, indications for colonoscopy, polyp types (pedunculated, sessile, or flat), site, size, histopathologic types, and grading of dysplasia, were collected by manually reviewing the files. Polyp sites were classified as proximal (cecum, ascending colon, and transverse colon), distal (descending colon, sigmoid colon, and rectum), and bilateral (proximal and distal). Polyp size was categorized as <1 cm, 1-2 cm, and >2 cm. Polyp size measurement was determined by the endoscopist as compared to open biopsy forceps (≈ 0.5 cm). The patients with polyp/s were divided into background normal colon (colonoscopic report reveals normal colonic mucosa apart from polyp finding) and background abnormal colon (I. IBD or colitis of any cause; II. CRC, a known case or diagnosed at present colonoscopy; III. Polyposis syndromes of any types) groups. Patients used 4 liters of Polyethylene Glycol in divided doses for bowel preparation on the day before colonoscopy with a clear liquid diet, according to the American Society for Gastrointestinal Endoscopy Guidelines 2009.

Most reviewed reports did not provide a uniform or written score for the quality of colon preparation, so this study did not consider the quality of bowel preparation. Colonoscopy examinations were done under conscious sedation with Phenytoin and/or Diazepam (ASGE guidelines 2008) using EPK-i5000 (Pentax; Japan) and LUCERA CLV 260 (Olympus; Japan) high-image-resolution colonoscopies. They were performed by a board-certified gastroenterologist.

Polyp prevalence was defined as the number of colonoscopies in which one or more polyps had been detected divided by the total number of

colonoscopies. Adenoma prevalence (synonymous with adenoma detection rate) was defined as the number of colonoscopies in which one or more adenomas had been detected divided by the total number of colonoscopies. Adenoma of advanced pathology (AAP) was defined as adenoma >1cm or with villoglandular histology or high-grade dysplasia. The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request. The collected data was handled and analyzed by SPSS 23 software. The chi-square test was used for categorical data. All

analyses were done with 95% confidence intervals, and p-values less than 0.05 were considered statistically significant.

Findings

The total number of colonoscopies from January 1st, 2020, to March 30th, 2022, was 3,893. After excluding poorly prepared or failed colonoscopies for any reason, 399 patients were found; thus, the number of patients with colonoscopies eligible in this study was 3494.

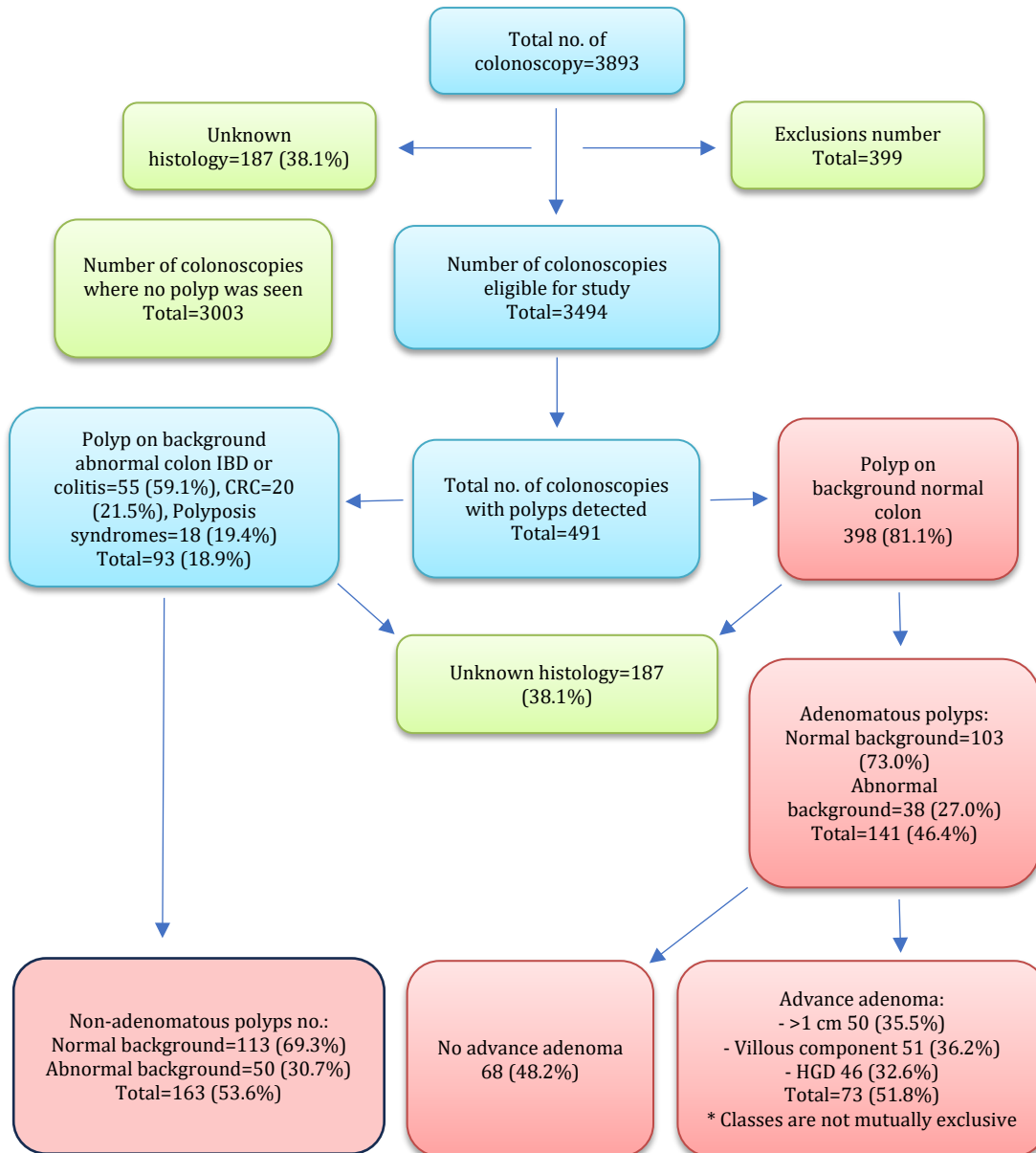


Figure 1. Baseline summary of the study characteristics

Males represented 1908 (54.6%), while females represented 1586 (45.4%). There were 3003 patients with colonoscopies with no polyp seen (including 820 with IBD or colitis and 141 with CRC) and 491 positive colonoscopies (with polyp). Those with polyps on background abnormal colon (IBD, CRC, and

polyposis syndromes) were 93 (18.9%). The other 398 (81.1%) were patients with polyp/s on background normal colon. Of 491 (total no. of patients with polyp), patients with inconclusive histopathology (normal mucosa), and patients with no histopathological report, which totaled 187

(38.1%), were excluded. From 141 (46.4%) adenomatous polyps, there were 103 (73%) with normal and 38 (27%) with abnormal colonic background. Non-adenomatous polyps were 163 (53.6%), 133 (69.3%) with normal and 50 (30.7%) with abnormal colonic background. There were 73 (51.8%) advanced adenomas, compared with 68 (48.2%) non-advanced adenomatous polyps (Figure 1). The most frequent presenting complaint in patients with polyps was bleeding per rectum (39.5%), followed by unexplained abdominal pain (19.6%), IBD or colitis (11.2%), constipation (6.9%), chronic diarrhea (5.1%), colorectal carcinoma (4.1%), polyposis syndrome (3.7%), altered bowel motion (3.5%), unexplained anemia (2.2%), family history of CA colon screening (2.0%), weight loss (1.0%), treated TB follow-up (0.6%), abdominal distension (0.4%), and colonic GIST on CT scan (0.2%).

The polyp detection rate was 16.3%, which increased with age, reaching the peak of 46.7% at 60 and above, with a disputing increase in PDR for patients under 20. The polyp detection rate in males (22.5%) was higher than in females (17.2%). The adenoma detection rate was 5.8%, with the highest 18.7% in patients ≥60 years old; in males, ADR was 5.9%, while in females, it was 5.6%. 187 patients (38.1%) with polyps had no defining histopathology. There was a significant relationship between age groups and type of lesion ($p < 0.001$). Still, there was no significant relationship between gender and type of lesion ($p = 0.086$). Also, there was a significant relationship ($p = 0.02$) between age groups and sites of lesions, as younger patients tended to have more distal lesions, some with multiple sites, and less proximal lesions, compared with older patients who had mostly distal, proximal, and multiple lesions (Table 1).

Table 1. Comparing the frequency (numbers in parentheses are percentages) of the patients according to age group and gender according to Polyp detection rate (PDR) and adenoma detection rate (ADR), type of lesion (non-adenomatous polyp-NAP/adenomatous polyp-AP) and location of the lesion (patients with colitis, colorectal carcinoma and polyposis syndrome were excluded)

Parameter	PDR	ADR	NAP	AP	Proximal	Distal	Multiple
Age group (year)							
1-9	(19.2)	(6)	19 (11.7)	1 (0.7)	4 (4)	24 (7.5)	1 (1.5)
10-19	(23)	(2)	14 (8.6)	3 (2.1)	0 (0)	25 (7.8)	8 (11.8)
20-29	(11.6)	(1.9)	15 (9.2)	5 (3.5)	5 (5)	17 (5.3)	8 (11.8)
30-39	(13.5)	(3.3)	26 (16)	16 (11.3)	14 (13.9)	44 (13.7)	7 (10.3)
40-49	(16.4)	(4.8)	27 (16.6)	25 (17.7)	15 (14.9)	61 (18.9)	9 (13.2)
50-59	(17.2)	(5.3)	31 (19)	30 (21.3)	24 (23.8)	60 (18.6)	13 (19.1)
≥60	(46.7)	(18.7)	31 (19)	61 (43.3)	39 (38.6)	91 (28.3)	22 (32.4)
p-Value (Chi-square)			<0.001		0.02		
Gender							
Male	(22.5)	(5.9)	107 (65.6)	79 (56)			
Female	(17.2)	(5.6)	56 (34.4)	62 (44)			
p-Value (Chi-square)			0.086				

Lesion types had no significant relationship with location ($p = 0.252$) and shape ($p = 0.243$). However, there was a significant statistical relationship between lesion types and corresponding sizes of lesions ($p < 0.001$; Table 2).

Table 2. Comparing the frequency (numbers in parentheses are percentages) of lesion types (non-adenomatous polyp-NAP=163; adenomatous polyp-AP=141) with their corresponding location, size, and morphology (Chi-square test)

Parameter	NAP	AP	p-Value
Location			
Proximal	38 (23.3)	29 (20.6)	0.252
Distal	104 (63.8)	84 (59.6)	
Multiple sites	21 (12.9)	28 (19.9)	
Size			
<1 cm	99 (60.7)	56 (39.7)	<0.001
1-2 cm	30 (18.4)	26 (18.4)	
>2 cm	26 (16)	37 (26.2)	
Variable sizes	8 (4.9)	22 (15.6)	
Morphology			
Pedunculated	39 (23.9)	38 (27)	0.243
Sessile	123 (75.5)	99 (70.2)	
Flat	1 (0.6)	4 (2.8)	

No significant relationship existed between sites and

their corresponding histopathology ($p = 0.49$). All types of polyps were found most commonly in the distal colon. Three cases of malignant colorectal polyp MCRP (adenocarcinoma; 0.9%) were also found in the distal colon.

Also, there was no significant relationship between types of adenomas and their corresponding sites ($p = 0.249$), as again, all types were commonly seen in the distal colon (Table 3).

The commonest lesions were retention polyps in 1-9 years (55.2%), inflammatory pseudopolyp in 10-19 years (21.2%) and 20-29 years (23.3%), and adenomatous polyps in 30-39 (24.6%), 40-49 (29.4%), 50-59 (30.9%), and over 60 (40.1%) groups. There was no significant relationship between the grade of adenomas and age groups ($p = 0.249$). Also, there was no significant relationship between the grade of adenomas and their corresponding sites ($p = 0.131$). However, the grade of dysplasia had significant relationships with their corresponding shapes ($p = 0.014$) and their corresponding sizes ($p < 0.001$; Table 4).

Table 3. Comparing the frequency (numbers in parentheses are percentages) of lesion location with their histopathology and histological type (Chi-square test)

Parameter	Proximal	Distal	Multiple	p-Value
Histopathology				
Inconclusive (normal mucosa)	6 (5.9)	18 (5.6)	1 (1.5)	0.49
Adenomatous	29 (28.7)	84 (26.1)	28 (41.2)	
Hyperplastic	9 (8.9)	21 (6.5)	7 (10.3)	
Retention	8 (7.9)	28 (8.7)	3 (4.4)	
Inflammatory pseudopolyp	18 (17.8)	44 (13.7)	9 (13.2)	
Hamartomatous	1 (1)	6 (1.9)	1 (1.5)	
Mucosal polyp	1 (1)	1 (0.3)	1 (1.5)	
No report for histopathology	28 (27.7)	116 (36)	18 (26.5)	
Sub-mucosal lipoma	1 (1)	1 (0.3)	0 (0)	
MCRP (adenocarcinoma)	0 (0)	3 (0.9)	0 (0)	
Histological type*				
Tubular	16 (33.3)	24 (50)	8 (16.7)	0.249
Tubulo-villous	6 (14)	27 (62.8)	10 (23.3)	
Villous	1 (12.5)	5 (62.5)	2 (25)	

*42 of the adenomas had an undetermined histological type.

Table 4. Comparing the frequency (numbers in parentheses are percentages) of the grade of adenomatous polyps' dysplasia (low=84; high=57) with age, location, morphology, and size of the lesion (Chi-square test)

Parameter	Low	High	p-Value
Age groups			
1-9	1 (1.2)	0 (0)	0.21
10-19	3 (3.6)	0 (0)	
20-29	1 (1.2)	4 (7)	
30-39	7 (8.3)	9 (15.8)	
40-49	17 (20.2)	8 (14)	
50-59	18 (21.4)	12 (21.1)	
≥60	37 (44)	24 (42.1)	
Location			
Proximal	22 (26.2)	7 (12.3)	0.131
Distal	47 (56)	37 (64.9)	
Multiple sites	15 (17.9)	13 (22.8)	
Morphology			
Pedunculated	16 (19)	22 (38.6)	0.014
Sessile	64 (76.2)	35 (61.4)	
Flat	4 (4.8)	0 (0)	
Size			
<1 cm	45 (53.6)	11 (19.3)	<0.001
1-2 cm	13 (15.5)	13 (22.8)	
>2 cm	14 (16.7)	23 (40.4)	
Different sizes	12 (14.3)	10 (17.5)	

Discussion

This study aimed to estimate the prevalence of colorectal polyps and adenomas and evaluate its relation to patients' age and polyp histopathology. Two-thirds of all colon polyps are adenomas, which, by definition, are dysplastic and have the potential for malignant transformation. Nearly all CRCs arise from adenomas, but only a small minority of adenomas will progress to cancer [15].

The outcome of our study showed that PDR was 16.3%, increasing with increasing age, reaching a peak of 46.7% at age 60 and old and slightly more in males (22.5%) than in females (17.2%), which is comparable with Almadi *et al.* [16], that PDR was 20.8% and 31.8% in patients ≥60 years old. Among the Iranians, a PDR of 16.5% was recorded [17], still much lower in Western countries than in the United States of America; the Mayo Clinic revealed a mean PDR of 49% [18].

Worldwide varies in adenoma prevalence with different populations [19]; in this study, adenoma detection rates were 5.8% highest (18.7%) at age ≥60 years old, with significant association with increasing

age and can be regarded as risk factors independently associated with increase adenoma prevalence [19], with no difference between male and female. This is comparable with Almadi *et al.* [16], that report ADR was 8.1% with not much gender difference, and this was partially consistent with Sohrabi *et al.* [17], where ADR was 14.3% and the new study in Mainland China by Hong *et al.* [19], ADR was 13.3% highest at age ≥65 years old (27.3%) and increase with age was similar in both sex; But in another study which report colorectal adenoma (CRA) in all age group combined was more likely to occur in men than in women as shown by Corley *et al.* [20]. In the Western population, the benchmark ADR is 25% for males and 15% for females in those >50 years old [21]; it's much higher than what's reported in our locality.

This discrepancy and low rates might be due to different reasons. PDR is influenced by several factors [22] that are not noted in the database used in our study, e.g., withdrawal time and overall procedure time, the quality of bowel preparation, the quality of the endoscopic devices, and the expert endoscopist. Variability in indications for

colonoscopy, asymptomatic (screening) or symptomatic, and high or low risk for CRC in our study low level of screening colonoscopy (2% from all indications). All age group was included, and the bulk of patients included in this study are between ages 30-59 years (64%), in contrast to (13.3%) of those ≥ 60 years old, as adenoma prevalence increases with age, especially those ≥ 60 years old [23]. It seems that adenomas are less prevalent in Asian populations compared to Western ones [16].

In our study, more than one-third of 38.1% of patients with polyp detection had unknown histology, which surely affects adenoma prevalence. Older patients ≥ 50 years had mostly distal as well as proximal and multiple sites of lesions, in contrast to younger age groups, which tend to have more distal lesions and less proximal; this finding is consistent with what was reported by Sohrabi *et al.* A remarkable portion (54%) of adenomas was detected beyond the rectosigmoid and was not detected by sigmoidoscopy alone [17].

All histopathological types are common, and three MCRPs (all of them) were found in the distal colon. This is the same finding by Hong *et al.* [19] and comparable with Yamaji *et al.* [24], who found that the malignant tendency of polyps in old people was generally stronger on the left-side colon than on the right-side colon. However, at the follow-up examinations, the malignant potential of neoplasms on the right-side colon increased substantially in the old to reach the same level as that on the left-side colon [25-42].

Non-adenomatous polyp tends to have small < 1 cm size, while most polyps > 1 cm are adenomatous; despite adenomas showing higher variability in sizes compared to non-adenomatous polyps, these findings are consistent with Hong *et al.* [19] finding that patients with polyps > 2 cm were higher in patients with adenomatous polyps than patients without and show the proportion of adenomatous polyps was 99.8% in patient groups with ≥ 1 cm polyps.

The commonest polyps seen in patients < 30 years are retention and inflammatory pseudopolyp; in contrast, adenomatous one emerges as the most frequent polyp detected at age ≥ 30 . This is a comparable finding with Almadi *et al.* [16] and Hong *et al.* [19].

We report that tubular as well as tubulovillous adenomas (48.4 and 43.4%, respectively) are nearly equally common and more frequent findings than villous type; this is inconsistent with Al-AlKhazraji *et al.* [43], which showed that tubular type much more common than the tubulovillous type (40% vs. 20%), but our result is similar to what was found in two previous Iraqi studies [44, 45] were tubular and tubulovillous are both common (34.4 and 62.4%, respectively). These findings should be considered and might need to be endorsed by large multicenter studies.

There was a significant association between the grade of dysplasia with morphological type and the size of the polyp, as pedunculated polyps and polyp size ≥ 1 cm were strongly associated with high-grade dysplasia ($p < 0.0003$). This was consistent with Silva *et al.* [44] in Brazil, who showed that polyps > 1 cm tended to be pedunculated and were more likely to exhibit an adenomatous component, a villous component, and dysplasia and also with Hong *et al.* [19], showed that the proportion of advanced-stage adenomatous polyps was 100% in patient with ≥ 1 cm polyp size.

This study recommends proper polyp handling during and after polypectomy and through specimen processing in the histopathological department; multicenter studies are needed to confirm the presence of a high percentage of advanced adenoma and to know more about adenoma characteristics and to estimate the cutoff age eligible for screening in Iraqi population. There is a need to develop a screening program in Iraq with colonoscopy as the first modality used because polyp/s in the proximal colon are common at age ≥ 50 years.

Conclusion

Increasing age is associated with an increased prevalence of colorectal polyps, especially adenoma, with male predominance. Tubulovillous adenoma and adenoma with advanced pathology are common findings. Over 1cm pedunculated polyps are associated with high-grade dysplasia.

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Ethical Permissions: The study was approved by the Ethics Committee of the Iraqi Council of Gastroenterology and Hepatology, Baghdad, Iraq, and by the Ethics Committee of the College of Medicine, University of Basrah, Basrah, Iraq.

Conflicts of Interests: Authors have declared that no competing interests exist.

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