Utility of Routine Terminal Ileoscopy and Biopsy During Colonoscopic Examination

Mohamed A. Mohamed a, Mohamed A. Metwally a, Khaled R. Zalata b, Hatem S. Alegaily A, Amr M. Abd-Elati A, Ahmed S. Elgazar a

 ^a Gastroenterology, Hepatology and Infectious Diseases
 Department, Faculty of Medicine Benha University, Egypt.

^b Pathology Department, Faculty of Medicine Benha University, Egypt.

Corresponding to:

Dr. Amr M. Abd-Elati.
Gastroenterology, Hepatology and Infectious Diseases Department, Faculty of Medicine Benha University, Egypt.

Email:

amrxonly2007@gmail.com

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Abstract:

Background: There is conflicting data to support routine terminal intubation and biopsies during colonoscopy. The clinical result may be predicted by the histological results of biopsies performed during terminal intubation. Aim of this work: to determine the utility of routine terminal ileoscopy (TI) and biopsy during colonoscopy in Hepatology, Gastroenterology and Infectious Diseases department at Benha University Hospitals, Benha, Egypt. Methods: This study was conducted on (140) consenting patients presented to colonoscopy Hepatology, Gastroenterology and Infectious Diseases department at Benha University Hospitals, because of one or more of the following complaints: Unexplained iron deficiency anemia, right lower quadrant (RLQ) abdominal pain, bleeding per rectum, positive occult blood in stool, chronic diarrhea and chronic constipation. Colonoscopy with routine terminal ileoscopy and biopsy was done for all patients. **Results:** 14/140 (10%) patients had either macroscopic 6/14 (42.9%)or microscopic 8/14 abnormalities of the terminal ileum while 3/14 (21.4%) patients had both. These were Crohn's disease (4/8), Behcet's disease (1/8), Tuberculosis (1/8), ileal villous atrophy (1/8) and nonspecific ileitis (1/8). 5/8 with macroscopically normal ileum had significant ileal abnormality: Crohn's disease (2/5), Tuberculosis (1/5), ileal villous atrophy (1/5) and nonspecific ileitis (1/5). Conclusion: Terminal ileoscopy and histopathological ileal examination improves the diagnostic yield of colonoscopy and influences management even in

endoscopically normal ileal findings.

Keywords: Colonoscopy, Ileoscopy, Right lower quadrant abdominal pain, Terminal ileal intubation.

Introduction

A test that is frequently used for both therapeutic and diagnostic purposes is the colonoscopy. For a number of years, it has been regarded as the gold standard for colorectal cancer screening (1). When diagnosing suspected inflammatory bowel disease (IBD), ileocolonoscopy, which includes doing terminal ileum biopsies, is crucial. It could help to rule out a number of inflammatory, infectious or functional conditions that could be mistaken for IBD (2). Exploration of the terminal ileum has rapidly gained the interest of international literature, starting from the first report in 1972 by Nagasako (3,4). There is conflicting data to support routine terminal intubation and biopsies during colonoscopy. A few trials have shown that for selected patients, terminal ileoscopy are beneficial (TI) and biopsy Histological results from TI biopsies might affect the clinical outcome in patients clinically suspected of having IBD and with a normal ileocolonoscopy (6). The majority of research on routine TI during colonoscopy has been done on populations in the West. Small number of studies on routine TI have been carried out in Asia or other tropical regions (5). The range of gastrointestinal illnesses varies in these areas; Crohn's disease (CD) comparatively rare while gastrointestinal infections, such as tuberculosis (T.B), are more common (7)

The aim of this study was to determine the prevalence of endoscopic and microscopic pathology in terminal ileum in patients undergo colonoscopy and to determine the utility of routine TI and biopsy during colonoscopy.

Patients and methods:

This cross-sectional prospective study was conducted on 140 consecutive patients attending Colonoscopy Unit in Hepatology, Gastroenterology and Infectious Diseases Department at Benha University Hospitals during the period from February 2022 to June 2023. After receiving approval from the Benha Faculty of Medicine Research Ethics Committee number:MD14.4.2021, the study was carried out. Each participant who was part of the study gave an informed consent.

Inclusion criteria:

Patients of both gender who were at least 18 years old attended the colonoscopy unit with one or more of the following complaints:

- 1-Unexplained iron deficiency anemia.
- 2-Chronic right lower quadrant (RLQ) abdominal pain.
- 3-Bleeding per rectum.
- 4-Positive occult blood in stool.
- 5-Chronic diarrhea.
- 6-Chronic constipation.

Exclusion criteria:

- 1- Patients presented to colonoscopy unit due to:
- A-Routine asymptomatic screening for colorectal carcinoma
- B-Follow up postoperative colectomy and post polypectomy.
- 2-Patient in whom colonoscopy revealed:
- A-Bleeding per rectum with obvious colonic cause (internal piles, diverticulosis, polyps, or masses) without any other macroscopic colonic mucosal lesions.
- B-Colorectal carcinoma or polyps without any other macroscopic colonic mucosal lesions.

Patients who met the inclusion and exclusion criteria had the following procedures: complete history taking and a careful clinical assessment. Laboratory studies in the form of CBC, liver profile test (prothrombin activity and INR, serum bilirubin (direct and total), serum albumin, serum alanine, and aspartate transaminase), kidney function tests, ESR, and CRP were participating patients done. All colonoscopy routine with terminal intubation and biopsy. The terminal ileum was considered endoscopically abnormal when ulcers, nodularity, strictures or

evidence of inflammation were reported by the endoscopist. Ileal biopsies were taken in all patients in whom ileoscopy was performed. Biopsy specimens were taken with multibyte biopsy forceps from lesions that were clearly visible or, in cases endoscopically normal ileum, from each quadrant of the terminal ileum that was at least five centimeters away from the ileocaecal valve. Other mucosal biopsies were taken from different sites in endoscopically normal colon or from obviously abnormal mucosal colonic areas. After administering midazolam or propofol for sedation, a colonoscopy was performed. Most procedures were done using Olympus 180 and FUJI EC 720 endoscopy units. Endoscopic biopsies were done in a wellequipped place under complete aseptic condition by highly qualified professors and a standard sheet was filled for every patient.

Statistical analysis:

The acquired data were updated, categorized, and tabulated with the use of the Statistical program for Social Science (IBM Corp. IBM SPSS Statistics for Windows, Version 25.0 (Armonk, New York: IBM Corporation, 2005). According to the kind of data collected from each parameter, the appropriate analysis was done on the given data. Using the Shapiro-Wilk test, the normality of the data distribution was examined. For regularly

distributed numerical data, descriptive statistics such as mean and standard deviation (SD) were computed; for non-normally distributed numerical data, median and range were determined. The frequency and proportion of nonnumerical data were determined.

Results

The patients in this study were 68 female (48.6%) and 72 males (51.4%), with a median age of 46 years. Of them, 52.1% were from urban areas and 47.9% were from rural areas. 58 cases (41.4%) were smokers. The most common indication for colonoscopy with ileal intubation was abdominal pain (32.1%) followed by hematochezia (25%), diarrhea (17.1%), constipation (14.3%), anemia (10%) and positive occult blood in stool (1.4%) (Table 1). A total of 14/140 (10%) out of patients had either macroscopic 6/14 (42.9%) or microscopic 8/14 (57.1%) abnormalities of the terminal ileum while 3/14 (21.4%) patients had both. Overall, 8/140 (5.7%) patients had a significant abnormal ileal histopathology, which influences management of patients or offered clinically helpful information: Ileal villous atrophy (1/8), Behcet's disease (1/8), TB (1/8), CD (4/8) and nonspecific ileitis (1/8) (Figure 1) and (Table 2).

Table (1): Indications for colonoscopy.

	N=140	%	
RLQ abdominal pain	45	32.14	
Diarrhea	24	17.14	
Bleeding per rectum	35	25	
Constipation	20	14.28	
Anemia	14	10	
Positive occult blood in stool	2	1.43	

RLQ: right lower quadrant.

Table (2): Microscopic abnormalities on ileoscopy of the terminal ileum.

Microscopic finding	N	%	
CD	4	50%	ulcerations with edematous villi, moderate inflammatory reactions in lamina properia with crypt abscess, sub mucosal fibrosis
Behcet disease	1	12.5%	superficial erosions with short villi, prominent eosinophilic infiltration and vasculitis
Т. В	1	12.5%	ulcerations, caseating granulomas, moderately infiltration by lymphoplasma cells and Langhans giant cells
Ileal_villous atrophy	1	12.5%	atrophy of the villi, lamina properia infiltration with predominant lymphocytes
Nonspecific ileitis	1	12.5%	normal villous pattern. lamina properia mildly edematous, moderately infiltrated by lymphoplasma cell with lymphoid aggregates, no granulomas
Total	8	100%	appropulation, no grandronido

CD: Crohn's disease T.B: tuberculosis

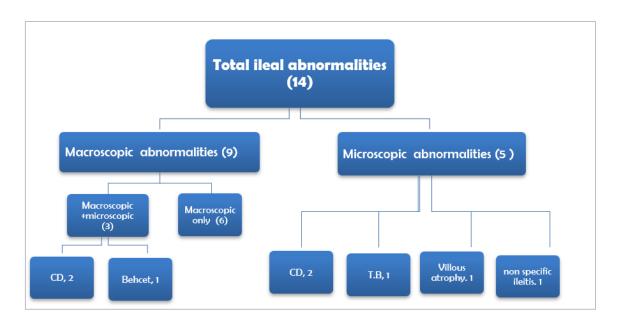


Figure 1: Macroscopic and microscopic abnormalities of the ileum.

Microscopic abnormalities of the terminal ileum were present in 6.7% of patients with RLQ abdominal pain, 16.7% of patients with diarrhea and 7.1% in patients with anemia (Table 3). 5/140 (3.6%) patients had significant ileal abnormal histopathological findings despite having normal terminal ileum at endoscopy. Among them there

were two patients with CD, one patient had TB, one patient had ileal villous atrophy and one patient had nonspecific ileitis (Figure 1). Macroscopic abnormalities of the terminal ileum (9/140 patients) described were ulcers 6/9 (66.7 %), erosions 2/9 (22.2%) or nodularity 1/9 (11.1%). Macroscopic abnormalities of

terminal ileum were present in 8.9% of patients with RLQ abdominal pain, 16.7% of patients with diarrhea and 2.9% in patients with hematochezia (Table 4). There were 6/140 (4.3%) patients with abnormal macroscopic appearance of the ileum but histology was normal on biopsy. Among them on ileoscopy, three patients had been described as having ileal ulcers, two patients had been found to have ileal erosions and other one patient had been found to have ileal nodularity. 137 out of 140 patients (97.8%) had no mucosal

abnormalities or abnormal histological findings of the colon on endoscopy. However, 6/137 (4.3%) of these patients had abnormal ileal histopathology (three patients had CD, one patient had T.B, one patient had ileal villous atrophy and one patient had nonspecific ileitis) on terminal intubation and routine histopathological ileal examination (Table 5). If TI and biopsy had not been carried out, the diagnosis for these patients would not have been made.

Table (3): Positive rates of microscopic abnormalities of terminal ileum according to indications for colonoscopy.

Indication	N (out of 140) (%)	Abnormal terminal ileum n (%)	CD (n)	Behcet (n)	T.B (n)	Ileal villous atrophy	Non specific ileitis
RLQ abdominal	45	3 (6.66%)	1	1	1	0	0
pain							
Diarrhea	24	4 (16.66%)	3	0	0	1	0
Bleeding per	35	0 (0%)	0	0	0	0	0
rectum							
Constipation	20	0 (0%)	0	0	0	0	0
Anemia	14	1 (7.14%)	0	0	0	0	1
Positive occult	2	0 (0%)	0	0	0	0	0
blood in stool		, ,					
Total	140	8 (5.71 %)	4	1	1	1	1

RLQ: right lower quadrant.

Table 4: Positive rates of macroscopic abnormalities of terminal ileum according to indications for colonoscopy.

Indication	N (out of	Abnormal terminal	Ulcer	Erosion	Nodula	
	140) (%)	ileum n (%)	(n)	(n)	r	
					(n)	
RLQ abdominal pain	45	4 (8.88%)	3	1	0	
Diarrhea	24	4 (16.66%)	2	1	1	
Bleeding per rectum	35	1 (2.85%)	1	0	0	
Constipation	20	0 (0%)	0	0	0	
Anemia	14	0 (0%)	0	0	0	
Positive occult blood in	2	0 (0%)	0	0	0	
stool						
Total	140	9 (6.42%)	6	2	1	

RLQ: right lower quadrant.

Table 5: Patients with macroscopic and microscopic findings of clinical importance of the terminal ileum.

No	Age/Sex	Indication	Macroscopic	Macroscopic	Microscopic	Microscopic
	O		ileal findings	colonic findings	ileal findings	colonic findings
1	49/Male	RLQ abdominal pain	Ulcers	Ulcers	CD	CD
2	41/Female	Diarrhea	Ulcers	Negative	CD	Negative
3	28/Female	Diarrhea	Negative	Negative	CD	Negative
4	39/Male	Diarrhea	Negative	Negative	CD	Negative
5	28/Male	RLQ abdominal pain	Ulcers	Ulcers	Behcet	Behcet
6	55/Male	RLQ abdominal pain	Negative	Negative	T.B	Negative
7	48/Male	Diarrhea	Negative	Negative	Ileal villous	Negative
					atrophy	
8	32/Male	Anemia	Negative	Negative	Nonspecific	Negative
					ileitis	
9	65/Female	RLQ abdominal pain	Ulcers	Negative	Negative	Negative
10	30/Female	RLQ abdominal pain	Erosions	Negative	Negative	Negative
11	59/Male	Diarrhea	Erosions	Erosions	Negative	Negative
12	60/Female	Diarrhea	Nodular	Negative	Negative	Negative
13	50/Male	Diarrhea	Ulcers	Negative	Negative	Negative
14	40/Female	Bleeding per rectum	Ulcers	Negative	Negative	Negative

CD: Crohn's disease

T.B: tuberculosis

RLQ: right lower quadrant

Discussion:

A test that is frequently used for both therapeutic and diagnostic purposes is the colonoscopy. For a number of years, it has been regarded as the gold colorectal cancer standard for When diagnosing screening suspected inflammatory bowel disease ileocolonoscopy, (IBD), which includes doing terminal ileum biopsies, is crucial. It could help rule out a number of inflammatory, infectious, or functional conditions that could be mistaken for IBD (2). According to studies, terminal intubation takes only three minutes added on the time of colonscopy (8). Moreover, there are no extra complications beyond those that arise with the colonoscopy (9). There is conflicting data to support routine terminal intubation and biopsies during colonoscopy. Therefore, this study was done to determine the prevalence of endoscopic and microscopic pathology in terminal ileum in patients undergo

colonoscopy and to determine the utility of routine terminal ileoscopy (TI) and biopsy during colonoscopy. This cross-sectional prospective study 140 consecutive patients involved University presented to Benha Hospitals' colonoscopy unit, Hepatology, gastroenterology and infectious diseases departments, participating Benha. Egypt. All patients had colonoscopy with routine terminal intubation and biopsy. The considered terminal ileum was endoscopically abnormal when ulcers, nodularity, strictures or evidence of inflammation were reported by the endoscopist. Ileal biopsies were taken in all patients in whom ileoscopy was performed. Biopsy specimens were taken with multibyte biopsy forceps from lesions that were clearly visible or, in cases endoscopically normal ileum, from each quadrant of the terminal ileum that was at least five centimeters away from the ileocaecal endoscopically normal colon or from obviously abnormal mucosal colonic areas. There were 68 male and 72 female patients in this study with a mean age of 46 years. In this study, RLQ abdominal pain (32.1%) was the common reason most for colonoscopy with ileal intubation, followed by hematochezia (25%), constipation (14.3%),diarrhea (17.1%), anemia (10%), and positive occult blood in stool (1.4%). This agrees with a prior study, which found abdominal pain (26.2%),that hematochezia (25%),constipation (14.1%), and diarrhea (14.1%) were the most common indications for colonoscopy with ileal intubation (10). However, a prior study found that abdominal pain accounted for 51.6% of the indications for a colonoscopy with ileal intubation followed by haematochezia (24.16%), constipation (10%), diarrhea (5.9%), and probable irritable bowel syndrome (4%) (11). In this study a total of 14/140 (10%) out of patients had either macroscopic 6/14 (42.9%) or microscopic 8/14 (57.1%) abnormalities of the terminal ileum while 3/14 (21.4%) patients had both (**Figure 1**). Overall 8/140 (5.7%) patients were diagnosed to have significant ileal pathology that changed the management of the patient or provided clinically useful information: CD (4/8), Behcet's disease (1/8), TB (1/8), ileal villous atrophy (1/8) and nonspecific ileitis (1/8). This is in agreement with a previous study that showed that 81/764 (10.6%) patients that had colonoscopy with terminal ileum intubation had either macroscopic 34/81 (42%)or microscopic 47/81(58%) abnormalities of the terminal ileum while 20/81 (24.7%) patients had both& Overall 47/764 (6.15%)patients were diagnosed to have significant ileal

valve. Other mucosal biopsies were

different

sites

taken

from

pathology: CD (28/47), TB (6/47), ileitis due to resolving infection (8/47) drug-induced ileitis subsequently diagnosed as probable nonsteroidal anti-inflammatory druginduced ⁽¹²⁾. The results of this study are higher figures compared to a previous study that showed that a clinically significant histopathology was observed in four of a total 269 cases underwent colonoscopy with successful TI, giving a 1.5% diagnostic yield of routine TI and all four cases were CD (11). The reason for the low diagnostic yield was that ileal biopsies were taken only from macroscopic abnormalities and terminal intubation was performed on unselected patients. On the controversy all of our patients participated in this study symptoms or a clear indication of colonoscopy and in addition, ileal biopsy was performed regardless of the ileum's terminal endoscopic appearance. Also, this current study's results are higher than those of a prior which revealed that diagnostic yield of routine TI was as low as 0.3% (13). This low diagnostic due to that terminal vield was was performed intubation asymptomatic patients undergoing screening colonoscopy and there was a low rate of successful terminal ileal intubation (20 %). Furthermore, the current study's results are higher than those of a previous study which discovered that TI had a 4.6% diagnostic yield (14). The limited diagnostic yield in this study was due to the low rate of successful terminal ileal intubation (16.1%). According to this current study, 6.7% of patients with RLQ abdominal pain, 16.7% of patients with diarrhea and 7.1% of patients with anemia had microscopic abnormalities of the terminal ileum. This is consistent with a prior study which showed that abnormal terminal ileal histopathological findings were

significantly present in the groups of diarrhea (9.7%),(9.5%), abdominal pain (4.5%), and chronic diarrhea with abdominal pain (27.3%) (15). This is also consistent with a prior study which demonstrated that 10% of patients underwent virtual chromoendoscopy and high-definition colonoscopy for persistent nonbloody diarrhea had abnormal histological findings of the terminal ileum (16). This is not in agreement with a prior study, showed that microscopic abnormalities of the terminal ileum were present in 0.4% of patients with diarrhea, 0.3% of patients with hematochezia, and 1.8% with chronic lower patients abdominal pain (5). This low yield in that previous study was due to the low diagnostic yield of terminal intubation in that study (0.3%) and that ileal biopsies were taken only macroscopic abnormalities.

This current study showed that 5 out of 140 patients (3.6%) had abnormal ileal histopathological findings despite having normal macroscopic ileum on ileoscopy. Among them were two CD patients, one TB patient, one ileal villous atrophy patient, and one nonspecific ileitis patient. This is consistent with a prior study which found that 27/764 (3.53%) patients had significant abnormal ileal histopathological findings despite normal macroscopic findings on ileoscopy. Those were 18 patients had CD, 5 patients had infection-related ileitis, and 4 patients had drug-induced ileitis (12).

This is in line with previous studies evaluated the histopathological findings of terminal ileum biopsies in patients with macroscopically normal ileum on ileoscopy and found that histopathological abnormalities were present in 5.5%, 5.1%, and 5% of the patients respectively (15, 17, 18).

This current study showed that (9/140 patients) had macroscopic

abnormalities of the terminal ileum. Among them 6/9 patients (66.7%) had ulcers, 2/9 (22.2%) had erosions and 1/9 (11.1%) had nodularity. Compared to a previous study, macroscopic abnormalities of the terminal ileum were found in (54/269 patients), described as mucosal nodularity (40.7%), congestion and/or erosions (38.9%), and ulcers (20.4%) (11).

According to this current study, macroscopic ileal abnormalities were found in 8.9% of patients with RLQ abdominal pain, 16.7% of patients with diarrhea and 2.9% of patients with hematochezia. This is consistent with a prior study found that macroscopic abnormalities were described in 27/276 (9.8%)of patients with abdominal pain, 58/1058 (5.5%) of patients with diarrhea, 6/165 (3.6%) of cases that were followed up for known medical-surgical conditions, and 7/399 (1.8%) of patients with hematochezia

According to this current study, 6/140 (4.3%) patients had abnormal ileal macroscopic findings with normal histopathology. Three patients were reported to have ileal ulcers, two patients had ileal erosions and one patient had ileal nodularity. It is hard to explain the cause; it could have been because of the policy of "biopsy when uncertain" when the endoscopist was unsure of a macroscopic appearance, or it could be because of the subjective nature of some endoscopic reports. This is consistent with a prior study that showed that 34/764 (4.45%) patients were described to have abnormal macroscopic ileal findings on ileoscopy with normal histological examination (12).

According to this current study, 137 out of 140 patients (97.8%) had no mucosal abnormality or abnormal histological findings of the colon on endoscopy. However, 6/137 (4.3%) of these patients had a significant ileal

abnormality ΤI and on histopathological examination (three patients had CD, one patient had T.B, one patient had ileal villous atrophy and one patient had nonspecific ileitis s). If TI and biopsy had not been carried out, the diagnosis for these patients would not have been made. This is consistent with a previous study that found 82.46% of patients had no mucosal abnormality on colonoscopy, However, 1.9% of these patients had significant ileal abnormalities (CD, drug-induced ileitis, and ileitis caused by resolving infection) on TI and histopathological examination Compared to a previous study, 14% (8/57) patients had ileal abnormalities with a normal colonoscopy or barium enema. This may be due to the small number of patients conducted in this study (9).

Conclusion

Based on the results of this current study, we can conclude the prevalence endoscopic and microscopic of pathology in terminal ileum in patients undergo colonscopy was 10% and also that terminal ileal intubation and routine histopathological examination colonscopy during improves diagnostic yield of colonoscopy and management influences endoscopically normal ileal findings.

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