Role of Computerized Tomography Enterography in Diagnosis of Inflammatory Bowel Disease

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Abstract

Background: Crohn's disease (CD) and ulcerative colitis (UC) are two examples of chronic and relapsing gastrointestinal disorders known as "inflammatory bowel disease" (IBD). This study aims to evaluate the role of CTE in identifying intramural and extramural changes in IBD patients and yield more detailed data about the level and severity of the disease process, thus planning for an appropriate treatment protocol.

Methods: This cross-sectional study was conducted from January 2019 until December 2020. It included 30 patients (13 males, 17 females) with clinical manifestations of bloody diarrhea, abdominal pain and/or tenesmus. Then, all patients were subjected to MSCT enterography, results were interpreted, and statistical analysis was done.

Results: The present work demonstrates that CT enterography is a sensitive method to detect inflammatory conditions of the large bowel, the presence of colonic polyps, fistula, stricture and/or abscess, the involvement of small bowel as well as the presence of extra-intestinal finding, thus helping the physicians to make more informed treatment decisions for the patients. However, no single characteristic is particular for differentiation between CD and UC.

Conclusions: CTE is useful for assessing intramural and extra-intestinal involvement in CD and UC.

Keywords: Crohn's disease, ulcerative colitis, intramural and extra-intestinal involvement, CT enterography.

Background:

Inflammatory bowel disease (IBD) is a chronic idiopathic disease of the gastrointestinal (GI) tract that consists of two independent but linked intestinal disorders: CD and UC. It is thought to be caused by an excessive and inappropriate immune response to gut luminal microbes in genetically predisposed individuals exposed to environmental risk factors. However, the exact causes of IBD remain unknown despite recent developments that have shed much light on its molecular pathogenesis (1).

Although there are some clinical and physiologic similarities between UC and CD, the diseases are distinct. While chronic inflammation in UC is limited to the intestinal mucosa of the large intestine, inflammation in CD can occur anywhere along the GI tract and is frequently transmural, predisposing patients with CD to the development of fibro stenotic (stricturing) and

penetrating (fistulizing) phenotypes that are not seen in UC. In some cases, UC and CD cannot be distinguished, and a diagnosis of IBD unclassified (IBD-U) is made, even though the clinical features of IBD-U are similar to those of UC (1).

The most typical symptoms in UC patients included fecal urgency, blood and/or mucus in the stool, diarrhea, stomach pain, weight loss, and asthenia. Patients with CD were shown to have higher rates of abdominal pain and distension, appetite loss, nausea and vomiting, weight loss, anemia, asthenia, insomnia, perianal illness, fever, extra-intestinal presentation, oral thrush, and abdominal mass than UC patients. Compared to CD patients, UC patients were more likely to experience urgency, fecal incontinence, blood and/or mucus in the stool, tenesmus, and constipation (2).

Imaging is essential for making a diagnosis and evaluating IBD. The degree of intestinal involvement, the activity of the disease, and the complications of uncontrolled IBD can all be determined using a variety of imaging techniques (3).

This study aims to evaluate the role of CTE in identifying intramural and extramural changes in IBD patients and yield more detailed data about the level and severity of the disease process, thus planning for an appropriate treatment protocol.

Methods

Study Design

The present study is a one-year cross-sectional study conducted at Assiut University Hospital, Egypt, from the 1st of January 2020 to the end of December 2020.

The study included 30 patients (13 males, 17 females). All enrolled patients had clinical manifestations of IBD, such as bloody diarrhea, abdominal pain, and/or tenesmus, and were suspected to have IBD. Then, all patients were subjected to MSCT enterography.

Ethical Consideration

The study received ethical committee approval from the Faculty of Medicine, Assiut University, Egypt (IRB No. 171018). All patients had provided written informed consent. This research's results were only used for scientific purposes and not for any other aims.

Study Population

The inclusion criteria included ages ranging between 18 and 80 years who have either clinical manifestations of IBD and/or are suspected of having IBD by abdominal ultrasound.

Patients who are generally contraindicated for CT radiation, particularly pregnant women, and those with contraindications to contrast as impaired renal function and hypersensitivity, patients aged less than 15 years old, and those who refused to participate in the current study were also excluded.

Procedures:

- **Patient Preparation:**
  - All patients are instructed to fast for 8 to 12 hours before examination.
  - A renal function test was performed on all patients.
  - Patients were informed about the CT scan and how to hold breathing during examination when requested to ensure their cooperation.

- **CTE Technique:**
  - Patients were scanned using a "Siemens Emotion 16-detector 69940" spiral CT.
  - The scanning parameters were: tube voltage, 130 kV; tube current, 128-266 MA; slice thickness, 1.5 mm.
  - The scanning range started from the diaphragm and went down to the ischial tuberosity.
  - Before scanning, the patient was informed to take 500-800 ml of clear water to fill the gastrointestinal tract as a negative contrast agent.
  - During the scan, a power injector injected 1.5 mL/kg iopromide (Ultravist 300, Schering, Berlin, Germany) IV with a 3–4 mL/s rate.
  - Conventional CT uses positive enteral contrast agents and water-soluble solutions to show anomalies in the gut wall and extra luminal fluid collections and attenuate the intestine lumen.
  - Maximal small bowel enhancement on MDCT was obtained to be 50 s after administration of intravenous contrast. We, therefore, administer contrast intravenously during this enteric phase. Obtaining the enteric phase images started at 35s after the trigger mark (trigger threshold level was 100 Hounsfield unit (HU) [12, 13].
  - CTE combines IV contrast injection with large-volume enteral contrast distension of the small bowel. Usually, neutral enteral contrast agents are utilized, which dilate the intestinal lumen without opacifying it. When using these substances, areas of non-dispensability, such as strictures and mucosal augmentation patterns, are visible.
  - Patients consume 1350 mL of diluted oral positive contrast (Gastrografin), with a smaller volume needed for pediatric patients dependent on weight. Unlike conventional CT, CTE images are taken during the enteric (45–60s post-injection phase).

Interpretation of Images:

All radiological data were reviewed on a workstation (Syngo via 2010). Specialized gastrointestinal tract radiologists thoroughly evaluated every computed tomography enterography examination; each revised the radiological findings individually and compared them.

CT enterography findings were assessed thoroughly, including subtle mucosal hyper-enhancement, bowel wall thickening, bi-lamellar or tri-lamellar mural stratification, comb sign, and different complications.

Statistical Methods:

Data was collected and analyzed using SPSS (Statistical Package for the Social Science, version 22). Quantitative data were expressed as mean ± standard deviation (SD) or median (range) and compared using Mann Whitney U. While nominal data were given as a number (n) and percentage (%) and compared using Chi^2-test or Fisher Exact test. The P-value was set to be significant at level 0.05.

Results

The demographic and clinical data of the studied participants are summarized in Table 1.

The mean was 39.50±13.13 years (range 20 to 68) years. Among 30

studied cases, 13 (43%) were males and 17 (57%) were females. Abdominal pain and diarrhea were the most common clinical presentations, documented in 50%, followed by weight loss in 40%, melena in 33%, bleeding per rectum in 23%, and fever in only one case (3%). A positive family history of IBD was reported in one patient **(Table 1)**.

Table (1) Patient characteristics (n=30).

Variable name	N	(%)
Age (years)		
• Mean±SD	39.50±13.13	
• Median (range)	40 (20 – 68)	
Sex		
• Male	13	(43.3)
• Female	17	(56.7)
Clinical presentation		
• Melena	10	(33.3)
• Weight loss	12	(40.0)
• Diarrhea	15	(50.0)
• Bleeding per rectum	7	(23.3)
• Abdominal pain	15	(50.0)
• Fever	1	(3.3)
Positive family history	1	(3.3)

Data are presented as mean ± SD and median (range) or number (%).

MSCT enterography findings in the studied patients

According to the CTE, the most commonly involved part of the colon was the right colon 17 (57%), followed by the left colon 7 (23%), and diffuse involvement of the colon was reported in 6 cases (20%). As regards the length of involvement, no cases suffered from focal involvement (< 5 cm), 13 (43%) have segmental involvement (6-40 cm), and 17 (57%) have diffuse involvement (>40 cm). Rectal involvement was observed in 12 (40%) of the studied patients. 19 cases (63%) were mild, 9 cases (30%) were moderate, and only two cases (7%) were marked bowel wall thickening.

Halo sign was observed in 8 cases (27%) and peri-colonic fat stranding in 22 cases (73%). Lymph node involvement was negative in ten cases (33%), not suspicious in 13 cases (43%), and suspicious in seven cases (23%). Comb sign was observed in 19 cases (63%). Also, CT enterography was able to detect small bowel involvement, which is divided into no involvement, proximal duodenum, middle jejunum, and distal ileal loops, and overall involvement, the percentile prevalence of lesions among them were 10 (33%), 3 (10%), 1 (3%), 12 (40%) and 4 (13%), respectively **(Table 2).**

Table (2) CT characteristics of bowel lesions of all studied participants (n=30).

Variable name	N	(%)
Site of involvement		
• Right	17	(56.7)
• Left	7	(23.3)
• Diffuse	6	(20.0)
Length of involvement		
• Focal (< 5 cm)	0	(0.0)
• Segment (6-40 cm)	13	(43.3)
• Diffuse (>40 cm)	17	(56.7)
Rectal involvement	12	(40.0)
Degree of thickness		
• Mild (3 – 4 mm)	19	(63.3)
• Moderate (5 – 9 mm)	9	(30.0)
• Marked (> 10 mm)	2	(6.7)
Halo sign	8	(26.7)
Peri-colonic fat straining	22	(73.3)
Lymph node involvement		
• No	10	(33.3)
• Not suspicious (<1 cm)	13	(43.3)
• Suspicious (≥1 cm)	7	(23.3)
Mesenteric vessels (Comb sign)	19	(63.3)
Small intestine involvement		
• No small bowel involvement	10	(33.3)
• Duodenum	3	(10.0)
• Jejunum	1	(3.3)
• Ilium	12	(40.0)
• Most small bowels involved	4	(13.3)

Data are presented as numbers (%).

Regarding the extra-intestinal manifestation

CTE detects hepatomegaly in 6 cases. One case (8%) has mild hepatomegaly, and 5 cases (39%) have moderate hepatomegaly; ascites was seen in 8 cases (62%), one case (8%) has splenomegaly, another case (8%) has chronic calcular cholecystitis.

Also, CT enterography detects complications in 20 patients (67%) in the form of stricture in 18 (90%), polyps in 2 (10%), and one case (5%) fistula. No cases suffered from an abscess or sinus (Table 3).

Table (3) Other extra-intestinal findings and complications detected by CT of the studied participants (n=30).

Variable name	N	(%)
Extra-intestinal finding	13	(43.3)
• **Hepatomegaly**		
▪ Mild hepatomegaly	1	(7.7)
▪ Moderate hepatomegaly	5	(38.5)
• **Ascites**	8	(61.5)
• **Splenomegaly**	1	(7.7)
• **Other finding**		
▪ CCC	1	(7.7)
▪ Lung	1	(7.7)
▪ Ovarian cyst	1	(7.7)
Complications	20	(66.7)
• **Stricture**	18	(90.0)
• **Polyps**	2	(10.0)
• **Fistula**	1	(5.0)
• **Abscess**	0	(0.0)
• **Sinus**	0	(0.0)

Data are presented as numbers (%).

Demographic differentiation between CD and UC

Out of 30 IBD patients, 21 patients were diagnosed with CD and 9 cases of UC by CT enterography (**Table 4)**. No significant difference was observed between the two groups regarding age and sex (p=0.340 and 0.229). The clinical presentation of the studied cases was comparable between both studied groups with no significant difference between them except for melena which was more commonly seen in CD (10 cases (47%) versus 0 cases (0.0%), P=0.013) respectively, and bleeding per rectum which was more common in UC (2 cases (10%) versus 5 cases (56%), P=0.014) respectively (**Table 4).**

Table (4) Patients characteristics according to their provisional diagnosis (n=30).

Variable name	Provisional diagnosis				P-value
	Crohn's disease (n=21)		Ulcerative colitis (n=9)		
Age (years)					0.340
• Mean±SD	37.76±13.45		43.56±12.08		
• Median (range)	32.0 (20 – 63)		42.0 (26 – 68)		
Sex					0.229
• Male	11	(52.4)	2	(22.2)	
• Female	10	(47.6)	7	(77.8)	
Clinical presentation					
• Melena	10	(47.6)	0	(0.0)	**0.013***
• Weight loss	7	(33.3)	5	(55.6)	0.418
• Diarrhea	10	(47.6)	5	(55.6)	1
• Bleeding per rectum	2	(9.5)	5	(55.6)	**0.014***
• Abdominal pain	9	(42.9)	6	(66.7)	0.427
• Fever	1	(4.8)	0	(0.0)	1
• Positive family history	0	(0.0)	1	(11.1)	0.300

Data are presented as mean ± SD and median (range) or number (%). *P-value* set significant at <0.05.

MSCT

The CTE was able to distinguish CD from UC as we observed that CD demonstrates higher small bowel involvement compared to UC (18 cases (86%) versus two cases (22.2), P=0.002) respectively **Table (5).**

Table (5) CT characteristics of bowel lesions of the studied participants according to their provisional diagnosis (n=30).

Variable name	Provisional diagnosis				P-value
	Crohn's disease (n=21)		Ulcerative colitis (n=9)		
Small bowel involvement	18	(86.0)	2	(22.2)	**0.002***
Site of colon involvement					
Right colon	17	(81.0)	0	(0.0)	
Left colon	0	(0.0)	7	(77.8)	**<0.001***
Diffuse colon involvement	4	(19.0)	2	(22.2)	
Length of involvement					
Focal < 5 cm	0	(0.0)	0	(0.0)	
Segment 6-40 cm	13	(61.9)	0	(0.0)	**0.003***
Diffuse >40 cm	8	(38.1)	9	(100.0)	

Variable name	Provisional diagnosis				P-value
	Crohn's disease (n=21)		Ulcerative colitis (n=9)		
Rectal involvement					0.102
No	15	(71.4)	3	(33.3)	
Yes	6	(28.6)	6	(66.7)	
Degree of thickness					0.841
Mild	14	(66.7)	5	(55.6)	
Moderate	6	(28.6)	3	(33.3)	
Marked	1	(4.8)	1	(11.1)	
Halo sign					0.374
No	14	(66.7)	8	(88.9)	
Yes	7	(33.3)	1	(11.1)	
Peri-colonic fat straining					0.374
No	7	(33.3)	1	(11.1)	
Yes	14	(66.7)	8	(88.9)	
Lymph node involvement					0.874
No	6	(28.6)	4	(44.4)	
Not suspicious <1 cm	10	(47.6)	3	(33.3)	
Suspicious ≥1 cm	5	(23.8)	2	(22.2)	
Mesenteric vessels (Comb sign)					0.100
No	10	(47.6)	1	(11.1)	
Yes	11	(52.4)	8	(88.9)	

Data are presented as numbers (%). P-value set significant at <0.05.

Another two characteristics of the lesions help to differentiate CD from UC lesions. The first is the site of bowel involvement. The CD demonstrates the involvement of the right colon in 81% or extensive diffuse colon involvement in 19%; meanwhile, UC reflects the involvement of the left colon in 78% or extensive diffuse colon involvement in 22%, $P < 0.001$.

Second was the length of wall involvement, as CD tends to cause segmental in 62% or diffuse wall involvement in 38%; meanwhile, UC tends to cause only diffuse wall involvement observed in All UC cases (P=0.003).

Other CTE characteristics such as rectal involvement, degree of thickness, halo sign, peri-colonic fat stranding, lymph node involvement, and mesenteric vessels (comb sign) show no significant difference between both studied groups (P=0.102, 0.841, 0.374, 0.374, 0.874 and 0.100), respectively.

There was no significant difference between the two groups regarding the extra-intestinal finding and the complications seen by the CTE (P=0.229 and 0.204), respectively.
(Table 6).

Table (6) Extra-intestinal findings and complications detected by CT of the studied participants according to their provisional diagnosis (n=30).

Variable name	Provisional diagnosis				p-value
	Crohn's disease (n=21)		Ulcerative colitis (n=9)		
Extra-intestinal finding	11	(52.4)	2	(22.2)	0.229
• Hepatomegaly	6	(100.0)	0	(0.0)	
• Ascites	6	(100.0)	2	(100.0)	
• Splenomegaly	1	(100.0)	0	(0.0)	
• Other finding	3	(100.0)	0	(0.0)	
Complications	12	(57.1)	8	(88.9)	0.204
• Stricture	11	(52.4)	7	(77.8)	
• Fistula	1	(4.8)	0	(0.0)	
• Polyps	1	(4.8)	1	(11.1)	

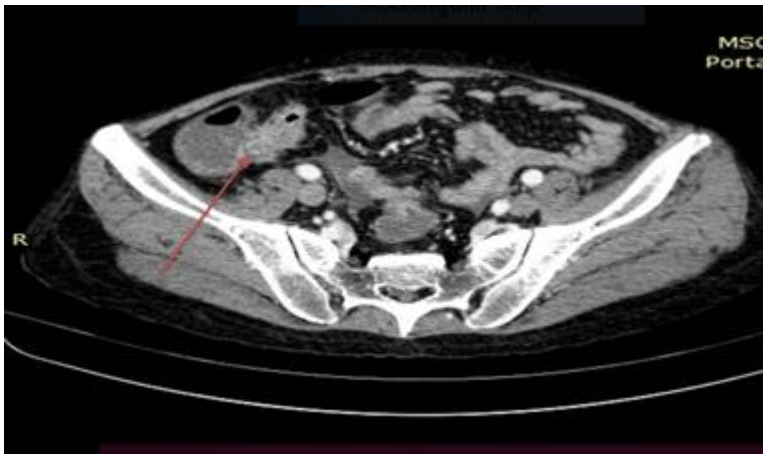
Data are presented as numbers (%). P-value set significant at <0.05.

Study limitations were due to the restricted statistical power of the small sample size; our study was done during the COVID-19 pandemic, and we could only identify significant differences in test performance. Also, our results did not evaluate the inflammatory activity of IBD.

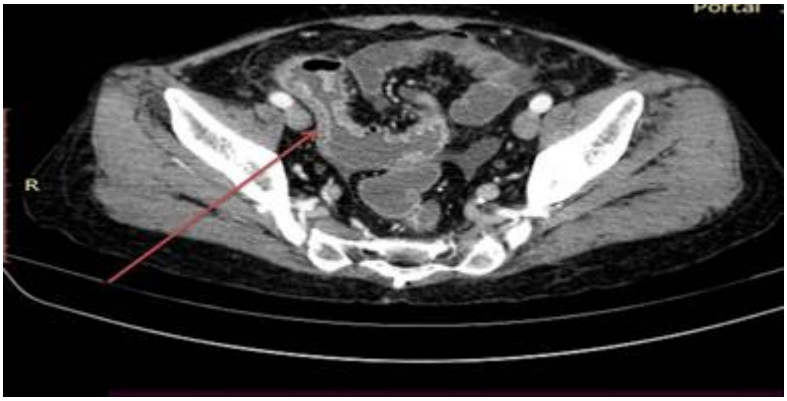
Figure Legends

Figure 1: A male patient, 32 years old, presented with abdominal pain, chronic diarrhea, and weight loss. AandB: thickening and enhancement of the cecum and illio-cecal valve with stricture segment at the illio-cecal valve, haziness and stranding of peri-colic fat, and prominent mesenteric vessels (arrows). C: enterography phase showing thickening and narrowing of the terminal ileal loops (arrow). D: A 3D image confirms these findings.

(A):



(B):

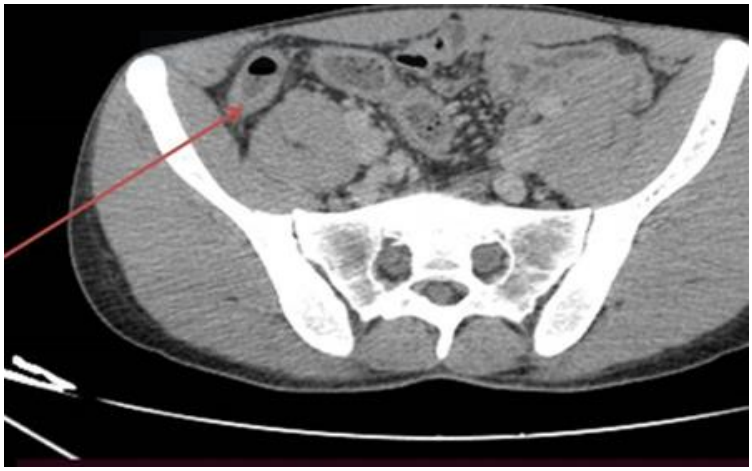


(C):

(D):

Figure 2: Male patient, 32 years old, presented with abdominal pain, tenesmus, bleeding per rectum, A, B, and C: MSCT diffuse thickening, mucosal enhancement of rectum, dilatation of vasa recta, and haziness of the perirectal fat planes and also sigmoid, descending with multiple stenotic segments and extend up to splenic flexure. D Enterography: normal.

(A):



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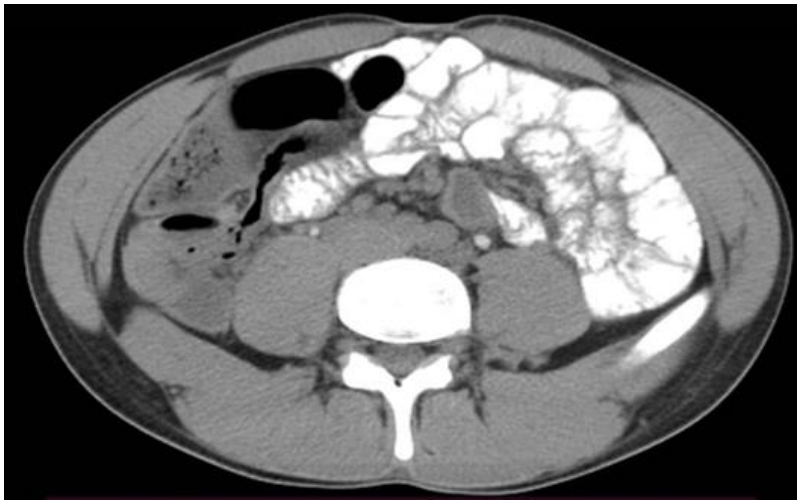
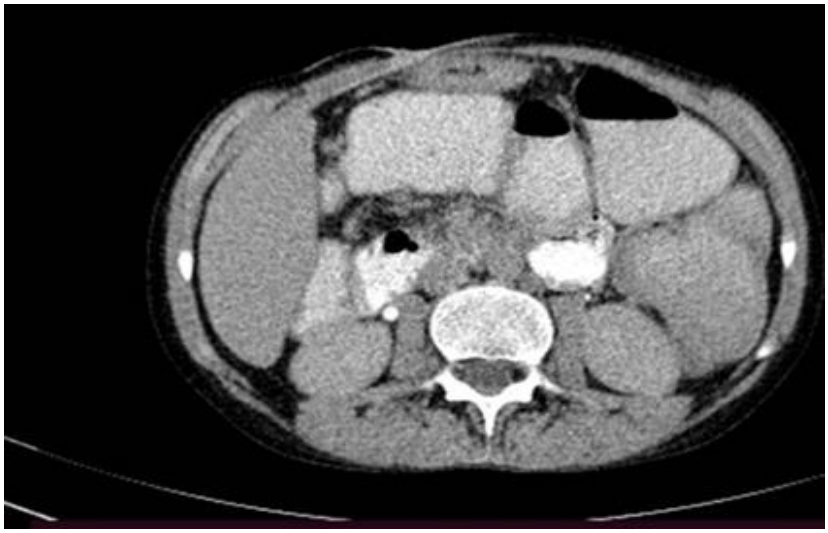


Figure 3: Male patient presented with chronic diarrhea, abdominal pain, and fever, a known case of Crohn's disease with a history of appendicectomy, right hemicolectomy, and resection anastomosis. A and B: MSCT with enterography shows a fistulous tract seen in the left iliac fossa; its internal orifice at the distal part of the descending colon, its external orifice at the external skin layer in the left iliac fossa (arrow). C: associated with edematous thickening of the ileal loops with preserved mural stratification with dilatation of other small loops (arrow).

Figure 3.A

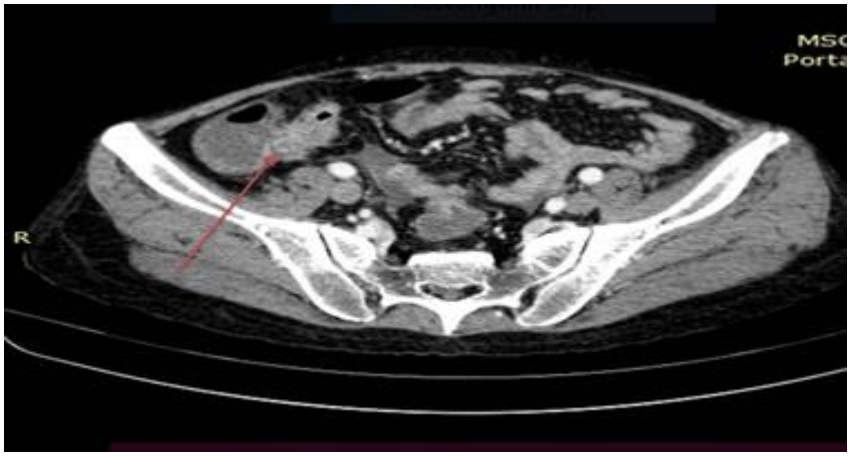
Figure 3.B:

Figure 3.C



Figures:

Figure 1.A:



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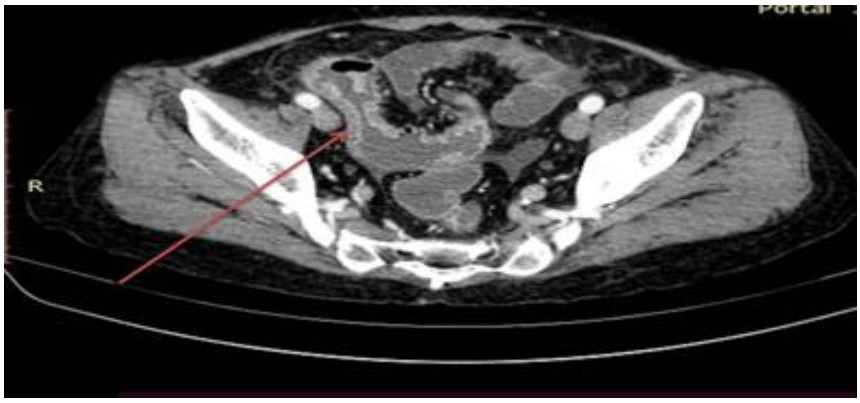
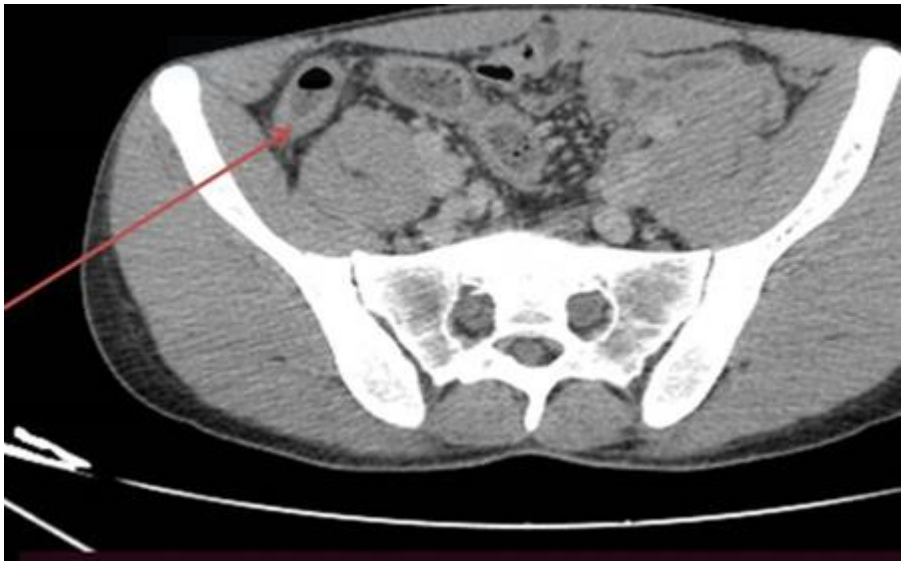


Figure 1.C:

Figure 1.D:

Figure 2.A:



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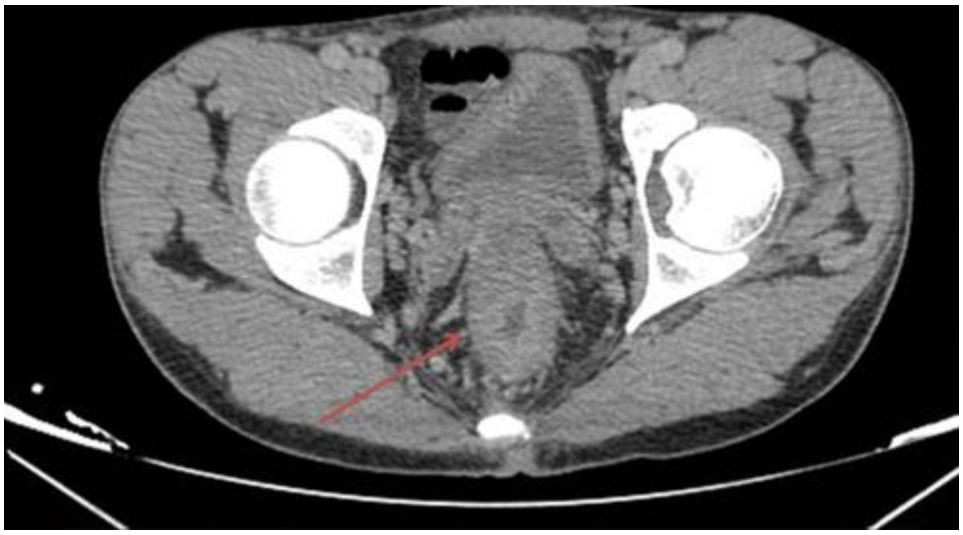
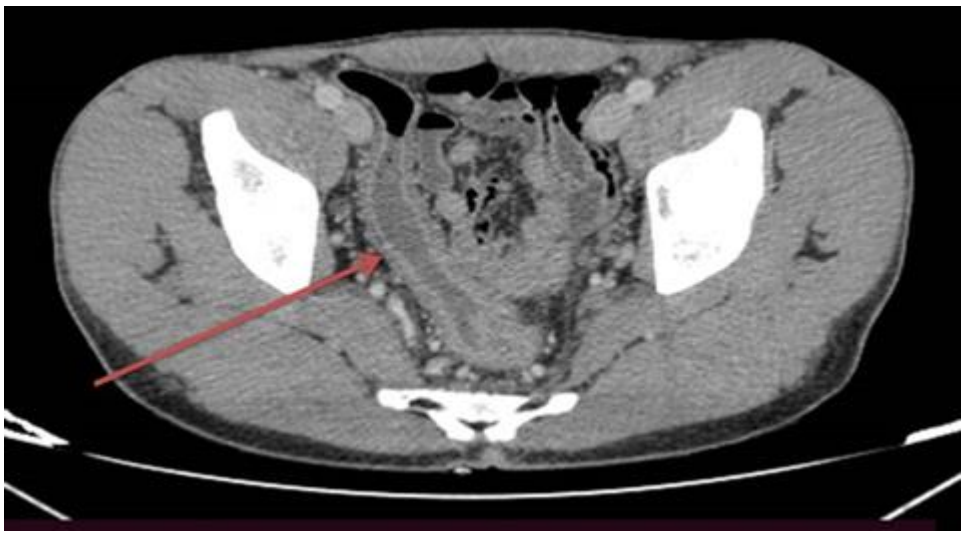


Figure 2.C



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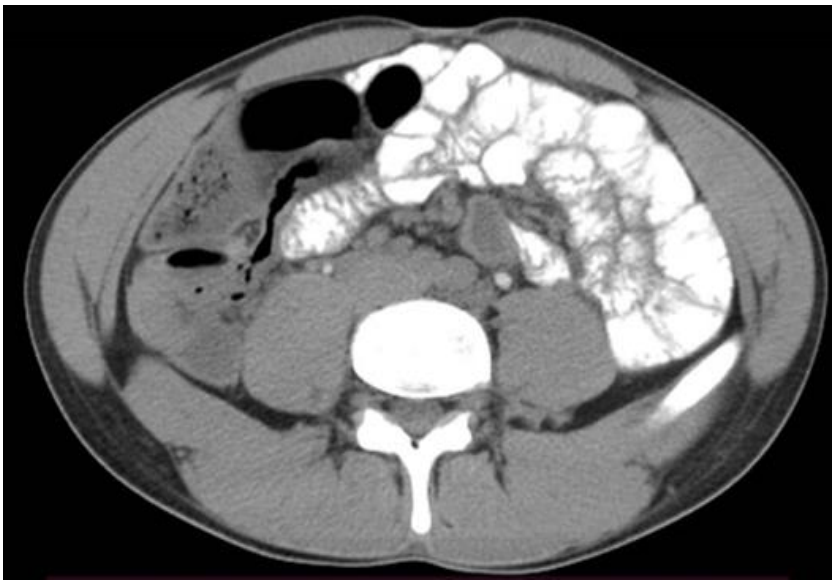


Figure 3.A

Figure 3.B:

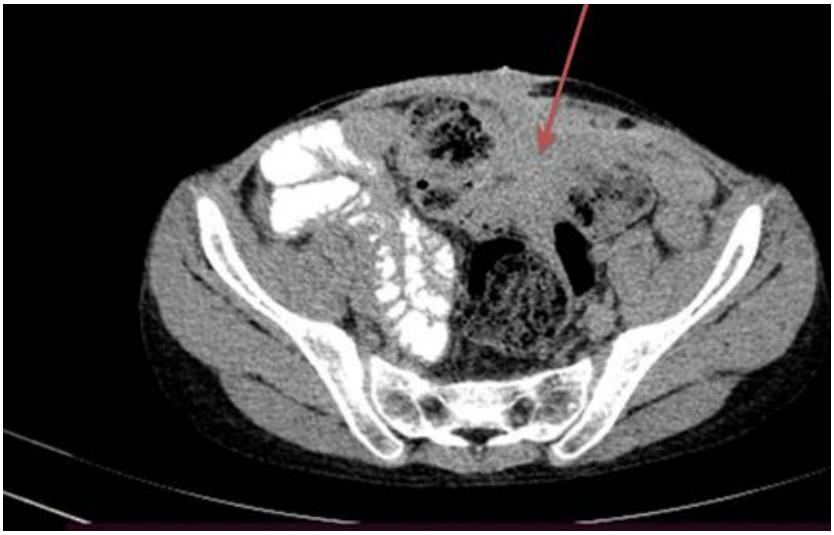
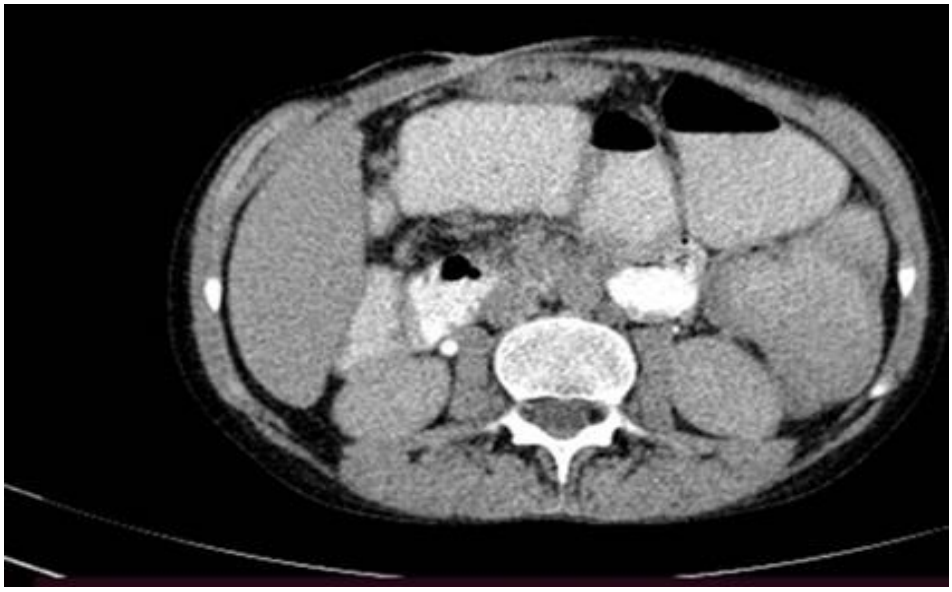


Figure 3.C



Discussion

The present work demonstrates that CTE is a sensitive method to detect inflammatory conditions of the large bowel, the presence of colonic polyps, fistula, stricture and/or abscess, the involvement of small bowel as well as the presence of extra-intestinal findings, thus enabling the doctors to decide on the best course of treatment for the patients with greater knowledge. However, there isn't a single trait that can be used to distinguish between CD and UC.

The most common clinical presentation among our studied cases was abdominal pain and diarrhea, which was found in 50%, followed by weight loss in 40%, melena in 33%, bleeding per rectum in 23%, and fever in only one case (3%). A positive family history was also observed in one case. El-Kalioubie and Ali reported a similar finding. They reported that all patients presented with chronic diarrhea, abdominal pain in 72%, loss of weight in 70%, and recurrent vomiting in 22% (5). Also, Ali and

Ghonimy reported that chronic diarrhea was the main presentation documented in 94%, while 82% presented with abdominal pain, 78% presented with loss of weight, and 20% presented with vomiting (6).

Our results show that the most commonly involved part of the colon was the right-sided colon; 43% had segmental involvement, 57% had diffuse involvement, and rectal involvement was observed in 40% of the studied patients. Bowel wall thickening was mild in 63%, moderate in 30%, and marked in 7%. Positive halo signs were observed in one-third of the cases we studied, and peri-colonic fat straining was observed in two-thirds of the patients we studied. Lymph node involvement was negative in 33%, not suspicious in 43%, and suspicious in 23%, and a positive comb sign was observed in 63.

Abd El Rasool et al., 2018(7) found that the prevalence of lesions of the duodenum, jejunum, and ileum involvement were 28%, 28%, and 44%,

respectively. The majority of intestinal lesions were found within the ileum. In the current study, CT enterography

was able to detect small bowel involvement, divided into no involvement, proximal duodenum, middle jejunum, distal ileal loops, and overall involvement. The percentile prevalence of lesions among them was 10 (33%), 3 (10%), 1 (3%), 12 (40%) and 4 (13%), respectively.

In addition, CTE helps evaluate and monitor the extra-intestinal manifestations of IBD. For example, CTE helps to detect hepatomegaly, ascites, splenomegaly, and chronic calcular cholecystitis and assesses in visualizing penetrating complications of the disease that extend outside the bowel wall. In our study, 67% have stricture, polyps, and fistula complications. This was in concordance with the study done by Abd El Rasool et al. (2018)(7), who reported that fistulae, strictures, and abscesses are detected by CTE at a rate of 96.3%, 61.6%, and 89.9%, respectively.

Our work aimed to differentiate between IBDs using a noninvasive technique (CTE). Out of 30 pathologically confirmed IBD patients, 21 patients were diagnosed with CD, and 9 were diagnosed with UC.

According to Elsayes et al. (2010) (8), mural enhancement is the most accurate sign of an active CD. Our analysis also revealed this.

Also, our results align with Patel et al.'s 2018 study (9), which reported that diffuse involvement was commonly seen in UC lesions.

Our results show that rectal involvement and bowel wall thickness show no significant difference between both studied groups. In contrast, Kalpesh K. Patel et al 2018;3. (10) observed that the most significant mean thicknesses of the colon wall were seen in CD patients.

A positive Halo sign was seen in 8 patients. There were seven cases with CD and only one with UC, with no significant difference.

Peri-colonic fat straining was seen in 22 (73%) of our cases as follows: 14 (64%) of them with CD and 8 (36%) with UC, with no significant difference between them. In contrast to our results, Philpotts et al., 1994(10) reported that submucosal fat deposition was present significantly more often in UC than in CD (P =0.0001).

Positive Comb sign was seen in 19 (63%) of our cases: 11 (58%) cases of CD and 8 (42%) cases with UC, with no difference between both groups (p=0.100). Abd El Rasool et al., 2018(7) observed Comb sign in 60% of cases with inactive UC and up to 8% of CD-diseased patients.

As regards complications, 20 (67%) of our cases suffered from different complications, stricture was seen in 18 (90%):11 (61%) cases of CD and 7 (39%) cases with UC, one case with CD complicated with fistula and polyps was seen in two cases; one case with CD and another one with UC, with no significant difference between both studied groups.

In conclusion, accurate IBD diagnosis is challenging and necessitates several tests. Diagnostic methods include medical history, physical examination, laboratory tests, endoscopy (including biopsy), and imaging studies. Currently, the best practices are endoscopy and biopsy. The only areas seen during a routine endoscopy are the colon and distal small bowel, making identifying small bowel disease challenging.

Conclusion

CTE enables the assessment of extra-intestinal manifestations and complications of IBD. However, many CT findings in patients with IBD are nonspecific.

List of Abbreviations

UC: Ulcerative Colitis.
IBD: Inflammatory Bowel Disease.
CD: Crohn's Disease.
US: Ultrasonography.
CTE: Computed Tomography Enterography.
CT: Computed Tomography.
MSCT: Multi-Slice Computed Tomography.
DM: Diabetes Mellitus.
TB: Tuberculosis.
IV: Intravenous.

Ethical Approval and Consent to Participate

After a detailed explanation of the study's goal and methods, each participant gave written informed consent to be included in the study. The University Hospital Institutional Review Board approved the study protocol. The clinical trials registration number was **ID: NCT03436966.**

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