

LEADING ARTICLE

Systematic reporting of computed tomography enterography/enteroclysis as an aid to reduce diagnostic dilemma when differentiating between intestinal tuberculosis and Crohn's disease: A prospective study at a tertiary care hospital

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Key words

Crohn's disease, computed tomography enteroclysis, computed tomography enterography, gastrointestinal tuberculosis.

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Abstract

Background and Aim: Crohn's disease (CD) and intestinal tuberculosis (ITB) have similar symptomatology and overlapping features on imaging, endoscopy, and histopathology. It is important to differentiate ITB from CD to initiate correct medical management. This prospective study aimed to characterize imaging features on computed tomography enteroclysis/enterography (CTE) that help in differentiating ITB from CD.

Methods: A total of 300 consecutive patients who underwent CTE with the suspicion of small bowel diseases were evaluated. CTE findings were documented on a detailed "CTE case record form" and were correlated with other investigations like endoscopy, histopathological and microbiological examination, and improvement on empirical therapy to arrive at a final diagnosis. Only confirmed cases of ITB/CD were included for further analysis.

Results: Final diagnoses revealed that 61 patients had ITB, 24 had CD, 90 patients had a final diagnosis not related to ITB/CD, and 125 had no bowel-related diseases. The sensitivity of CTE (ITB vs CD, 90.2 vs 91.6%) was higher than the sensitivity of ileocolonoscopy (ITB vs CD, 87 vs 83.3%). A homogenous pattern of bowel wall thickening and confluent bowel involvement were significantly more common in ITB. Stratified bowel wall thickening with mucosal hyperenhancement, skip lesions in the bowel, and a comb sign were significantly more common in CD. Stratified bowel wall enhancement with an intervening layer of fat was specifically ($P < 0.001$) seen in patients with CD, and necrotic ($P = 0.002$) and calcified ($P = 0.055$) lymph nodes were specifically seen in patients with ITB.

Conclusion: We propose a systematic approach to the radiological differentiation of ITB from CD.

Introduction

Infective diseases like intestinal tuberculosis (ITB) are a matter of concern in developing countries like India due to their high prevalence. ITB is similar to Crohn's disease (CD) regarding symptomatology, imaging, endoscopy, and histopathology.¹ Traditionally, barium studies were used to evaluate bowel lesions; however, they failed to demonstrate extraluminal findings.^{2–4} Nowadays, computed tomography (CT) with enteroclysis/enterography (CTE) using neutral oral contrast media is the investigation of choice for patients with suspected ITB or CD. CTE provides good bowel distention, which helps in disease localization and assessment of various

patterns of bowel wall enhancement and demonstrates the extraintestinal findings.^{5,6}

The final diagnosis of ITB or CD is usually made by correlating CTE findings with endoscopy, histopathology, or clinical/endoscopic improvement with empirical therapy. Ileocolonoscopy usually demonstrates transverse ulcers and a patulous ileocecal valve in ITB and mucosal cobblestoning and linear ulcers in CD.^{7–10} Histopathology shows caseating granulomas and acid-fast bacilli in ITB and fissuring ulcers and transmural inflammation in CD.¹¹ However, in practice, we rarely find a classical picture of these diseases on imaging, endoscopy, or histopathology, and more often than not, an overlap of the various findings exists.

Table 1 Distribution of diseases in the study sample

Final diagnosis on correlating CTE with other modalities	Distribution (n = 300)
No bowel-related disease	125 (41.6%)
Intestinal tuberculosis	61 (20.3%)
Crohn's disease	24 (8%)
Ulcerative Colitis	11 (3.6%)
Stricture of unknown etiology	25 (8.3%)
Bowel polyps	7 (2.3%)
Duodenal ulcers	3 (1%)
Infection- hydatid/amoebiasis/strongyloidiasis/ascariasis	5 (1.6%)
Appendicitis with or without appendicolith	8 (2.6%)
Malabsorption	5 (1.6%)
Malrotation	5 (1.6%)
Bowel neoplasms	21 (7%)
Total	300

CTE, computed tomography enteroclysis/enterography.

Thus, a systematic format-based approach for reporting CTE prevents misdiagnosis and helps in the early initiation of disease-specific medical management.

Methods

A total of 300 consecutive patients were prospectively evaluated from March 2016 to April 2018 with the approval of the Institutional Ethics Committee (IEC Code 2016-46-MD-90). Written informed consent was obtained from all the patients participating in the study. The inclusion criteria were:

Table 2 Summarizing the mode of diagnosis for patients of Crohn's disease and intestinal tuberculosis

Mode of diagnosis in patients with CD (n = 24) and ITB (n = 61)	Number of cases (n = 85)
Diagnosis of CD based on:	
CTE+ Symptomatology + Endoscopy	11/24 (45.8%)
CTE+ Symptomatology + Histopathology	8/24 (33.33%)
CTE+ Symptomatology + Response to CD-specific treatment after failure to respond to empirical ATT trial	3/24 (12.5%)
Endoscopy + Response to CD-specific treatment after failure to respond to empirical ATT trial with no evidence of bowel wall thickening on CTE	2/24 (8.3%)
Diagnosis of ITB based on:	
CTE+ Ancillary features specific to ITB on CTE + Endoscopy	20/61 (37.8%)
CTE+ Ancillary features specific to ITB on CTE + Histopathology	11/61 (18%)
CTE+ Response to empirical ATT trial	22/61 (36.06%)
Endoscopy + Histopathology with no evidence of bowel wall thickening on CTE	6/61 (9.8%)
Endoscopy + Response to empirical ATT trial with no evidence of bowel wall thickening on CTE	2/61 (3.3%)

ATT, antitubercular therapy; CD, Crohn's disease; CTE, computed tomography enteroclysis/enterography; ITB, intestinal tuberculosis.

Table 3 Comparison of clinical features between Crohn's disease and intestinal tuberculosis

Symptoms	Intestinal tuberculosis (n = 61)	Crohn's disease (n = 24)
Pain abdomen	23 (37.7%)	19 (79.2%)
Fever	45 (73.7%)	4 (16.6%)
Loss of weight	46 (75%)	1 (4%)
Loose stools	6 (9.8%)	17 (70.8%)
Melena	10 (16.3%)	8 (33.3%)
Loss of appetite	45 (73.7%)	1 (4%)
Vomiting	19 (31.1%)	6 (25%)
Distention of abdomen	6 (9.8%)	3 (12.5%)

(i) consecutive adult patients (>18 years) who underwent CTE for symptoms suggestive of ITB or CD; (ii) radiological investigations like ultrasound, barium studies, and/or chest X-ray/CT findings suspicious of tuberculosis or CD; (iii) lesions on ileocolonoscopy suspected to be due to ITB or CD (time duration between ileocolonoscopy and CTE was less than 2 weeks, and no medical treatment was started during this period); (iv) cytologically/histologically/microscopically proven ITB or CD based on ileocolonic biopsy or lymph node fine needle aspiration cytology (FNAC)/biopsy; and (v) patients with bowel lesions who showed clinical improvement with empirical treatment for ITB or CD. The exclusion criteria were patients with: (i) known adverse reaction to iodinated contrast media, (ii) history of gastrointestinal surgery, and (iii) final diagnosis of neither ITB or CD.

Computed tomography enteroclysis and enterography.

All patients were advised to be nil per oral at least 6 h before the examination. CT Enteroclysis: The nasal cavity was anesthetized with local anesthetic gel (Lox-2% Jelly, Neon Laboratories, Ltd., Mumbai, India), followed by insertion of a 12-16F nasojejunal (NJ) tube (Devon Innovations Pvt. Ltd., Bengaluru, India) under fluoroscopic guidance. The tip of the NJ tube was positioned in the proximal jejunum, and 1.75–2 liters of normal saline (NS) were infused through the NJ tube. CT Enterography: CT enterography was performed when the patients did not consent for NJ tube insertion

Table 4 Comparison of endoscopy/colonoscopy findings in patients with Crohn's disease and intestinal tuberculosis

Endoscopy findings	Intestinal tuberculosis (n = 61)	Crohn's disease (n = 24)	P*
Anorectal lesions	1 (1.6%)	5 (20.8%)	0.002
Longitudinal ulcers	1 (1.6%)	8 (33.3%)	<0.001
Skip lesions	4 (6.6%)	10 (41.6%)	<0.001
Aphthous ulcers	10 (16.4%)	11 (45.8%)	0.005
Patulous ileocecal valve	16 (26.2%)	1 (4.2%)	0.022
Transverse ulcers	22 (36.1%)	1 (4.2%)	0.002
Nodularity	15 (24.6%)	2 (8.3%)	0.133
Cobblestone appearance	1 (1.6%)	8 (33.3%)	<0.001

*P < 0.05.

or if the NJ tube insertion failed. Patients had to consume 2–2.5 L of iso-osmotic polyethylene glycol (PEG) solution approximately 45 min before the CT examination. CTE was performed using a multidetector CT scanner (Brilliance 64, Philips Healthcare, Amsterdam, Netherlands) from the level of the diaphragm to the lower edge of pubic symphysis. To improve bowel distension, 20 mg of intravenous (IV) hyoscine butyl bromide (Buscopan, Boehringer Ingelheim Pvt. Ltd., Mumbai, India) was administered before scanning. The scanning parameters were as follows: 120 KV, 200 mAs, detector configuration 64×0.6 , slice thickness of 3 mm, and 1.5-mm reconstruction interval. A noncontrast CT scan was first performed to access bowel distension. If the distension was inadequate, 250 mL of normal saline infusion was performed in CT enteroclysis, and for CT enterography, patients were advised to drink more PEG solution (250 mL). Contrast-enhanced CT was performed with nonionic iodinated contrast material (Iohexol 350 mg/mL- Omnipaque; GE Healthcare, Waukesha, WI, USA) (1.5 mL/kg) at the rate of 4 mL/s, and a scan was acquired 30–50 s after injecting IV contrast.

Stepwise evaluation of CTE on a case record form. Step 1- Abnormal small bowel loops were defined by a wall thickness of ≥ 3.0 mm.

Step 2- Assessment of the pattern of enhancement was carried out at the site where the bowel wall was maximally thickened. The following patterns of bowel wall enhancement were observed: (i) homogenous pattern (HP): bowel wall thickening with no distinct stratification pattern or any difference of the Hounsfield (HU) values from the mucosal to the serosal layer of the bowel wall; (ii) stratification with mucosal hyperenhancement (SMH) defined as “a type of stratified pattern of bowel wall enhancement with a hyper enhancing mucosal layer with or without a central hypodense layer which is not of fat attenuation,” and the HU value of the inner enhancing mucosal layer was documented; and (iii) stratification with an intervening layer of fat (SIF) defined as “a type of stratified pattern of bowel wall enhancement with an intervening middle layer of fat,” and the HU value of the middle layer of fat/hypodensity was documented.

Step 3- Location of thickening: (i) jejunum; (ii) duodenum; (iii) terminal ileum; (iv) confluent bowel involvement, defined as

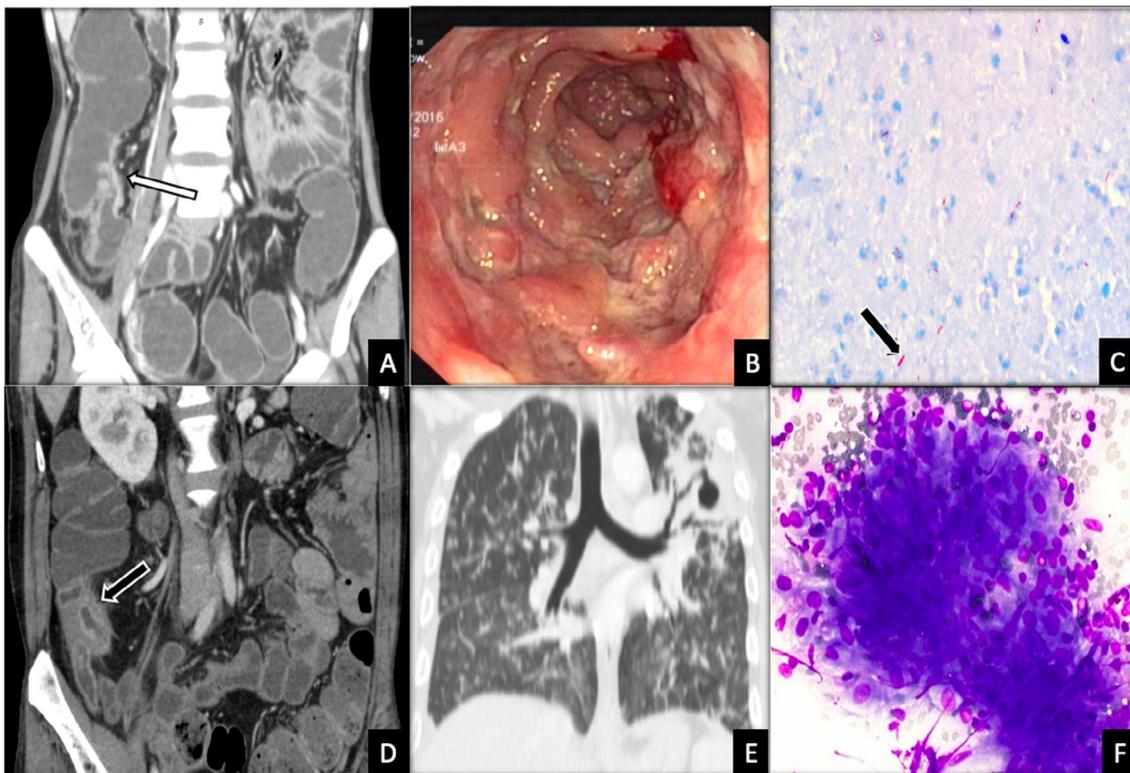


Figure 1 Computed tomography enterography of a 48-year-old man with final diagnosis of intestinal tuberculosis (ITB) (a–c). Coronal image (a) shows homogenous bowel wall thickening (white arrow) involving the ileocecal junction (ICJ); ileocolonoscopy (b) shows ulceronodular mucosa in transverse distribution at the ICJ; histopathology (c) shows acid-fast bacilli (black arrow) on Ziehl-Neelsen staining, 100 \times . Another 52-year-old lady with final diagnosis of ITB (d–f). Coronal image (d) shows stratification with mucosal hyperenhancement pattern of bowel wall thickening (black arrow) at terminal ileum and ICJ; lung window of chest computed tomography (e) shows a thick walled cavitary lesion in the left upper lobe with multiple tree-in-bud infiltrates; fine-needle aspiration cytology (f) of an enlarged cervical lymph node shows a granuloma comprising of epithelioid histiocytes and lymphocytes [May- Grunwald Giemsa (MGG) stain, 40 \times].

“thickening involving terminal ileum, ileocaecal junction (ICJ) and adjacent colon”; and (v) large bowel.

Step 4- Length of bowel segment involved: (i) long segment >50 mm; (ii) short segment <50 mm.

Step 5- Ancillary CTE findings: (i) necrotic nodes defined as “lymph nodes with reduced central density”—the HU value at the center of the lymph node was documented; (ii) associated lung findings (chest X-ray or chest CT) specific to tuberculosis; (iii) calcified abdominal lymph nodes; (iv) enteroliths; (v) peritoneal thickening defined as enhancing peritoneal thickening >1 mm; (vi) ascites; (vii) comb sign; (viii) skip lesions, “more than one non-contiguous sites of involvement in any part of the bowel”; (ix) fibrofatty proliferation; (x) enteroenteric/enterocutaneous fistula; and (xi) locoregional nonnecrotic lymph nodes defined as “locally enlarged lymph nodes near the affected bowel with uniform density and HU values at the centre and periphery of the node,” and the HU value at the center of the lymph node was documented; (xii) perianal lesions; and (xiii) stricture segment of bowel wall thickening with attenuation of luminal caliber and associated abnormal dilatation of the proximal bowel loops.

Step 6- Any other significant findings.

Two radiologists experienced in abdominal imaging performed the assessment of all the CTE images (double reading).

Final diagnosis of ITB. CT finding of bowel lesions along with at least one of the following criteria: (i) histological features

of caseating granulomas; (ii) histological investigation demonstrating acid-fast bacilli; (iii) *Mycobacterium tuberculosis* found on tissue culture; (iii) upper gastrointestinal endoscopy (UGIE) or ileocolonoscopy features suggestive of intestinal tuberculosis, like punched out/rodent-like or transverse ulcers and patulous ileocecal valve with proven tuberculosis elsewhere in the body, and (iv) patients with diagnostic dilemma who received empirical antitubercular therapy (ATT) and showed a good clinical response in the form of loss of subjective symptoms at 6 months' follow up.^{12,13}

Final diagnosis of CD. The final diagnosis of CD was based on the CT finding of bowel lesions along with at least two of the following three criteria (Japanese diagnostic criteria): (i) histopathological features suggestive of transmural inflammation and/or epithelioid granuloma; (ii) clinical symptoms of abdominal pain, weight loss, malaise, diarrhea, and/or rectal bleeding; and (iii) endoscopic findings of mucosal cobblestone ulcers, linear ulceration, skip areas, or perianal disease.^{14,15}

Patients who had no confirmed diagnosis of ITB or CD initially received empirical ATT for 6 months, and if they failed to show good response, CD-specific treatment was initiated. Patients with a good clinical response to this treatment were given a final diagnosis of CD.

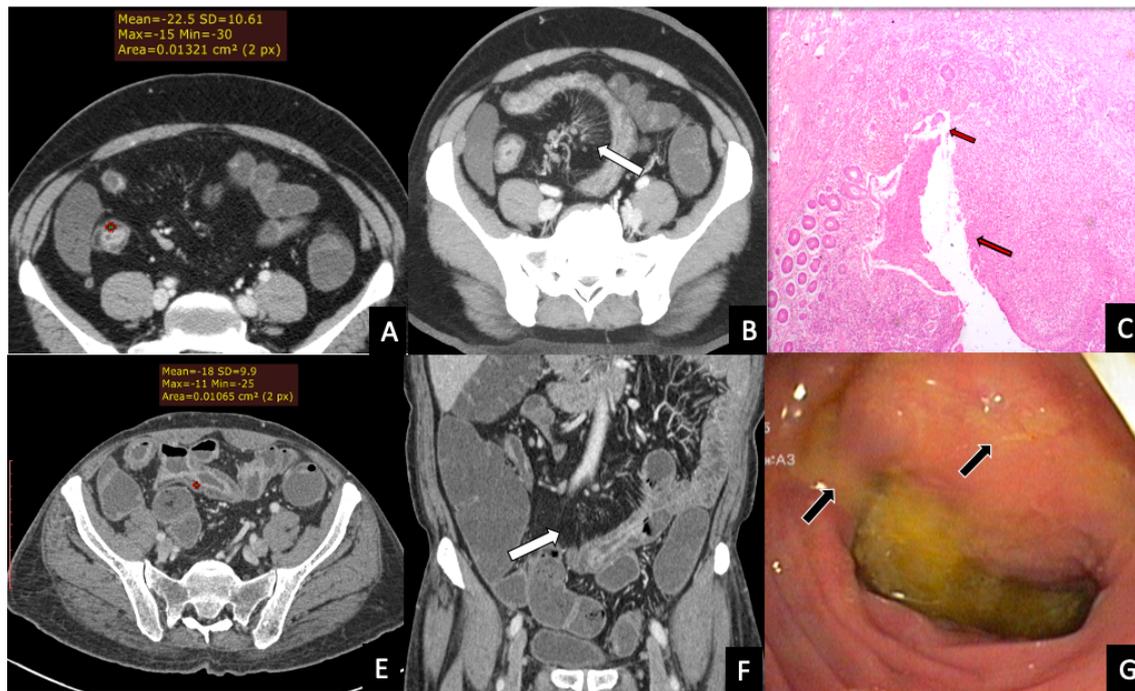


Figure 2 Computed tomography enterography of a 44-year-old lady with final diagnosis of Crohn's disease (CD) (a–c). Axial computed tomography (CT) (a) shows stratification with intervening layer of fat (SIF) pattern of bowel wall thickening involving distal ileum (red asterisk demonstrates fat density); maximum intensity projection image (b) shows comb sign (white arrow); histopathology (c) reveals fissure ulcer (red arrows) with surrounding inflammatory cells. Another 47-year-old lady with final diagnosis of CD (d–f). Axial CT (d) shows SIF pattern of bowel wall thickening involving distal ileum (red asterisk demonstrates fat density); coronal image (e) shows fibrofatty proliferation (white arrow) around the distal ileal loop; ileocolonoscopy (g) shows aphthous and white-based ulcers (black arrows).

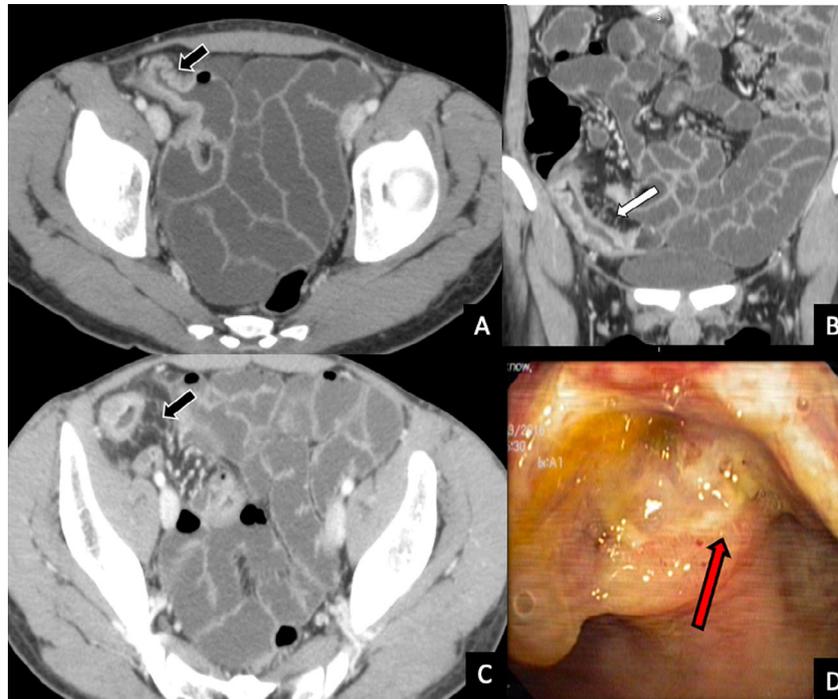


Figure 3 Computed tomography enterography of a 49-year-old man with final diagnosis of Crohn's disease. Axial image (a) shows stratification with mucosal hyperenhancement pattern of bowel wall thickening involving distal ileum (black arrow); maximum intensity projection image (b) shows comb sign (white arrow); axial image (c) shows fibrofatty proliferation (black arrow) around the involved distal ileal loop; ileocolonoscopy (d) shows multiple linear aphthous ulcers (red arrow).

Statistical evaluation was performed using SPSS software (version 21.0; SPSS, Inc., Chicago, IL, USA). CTE findings of ITB and CD were compared using the Pearson

chi-square test or Fisher's exact test. A "P" value of <0.05 was considered statistically significant. Kappa agreement and phi correlation coefficient were used to compare ileocolonoscopy and

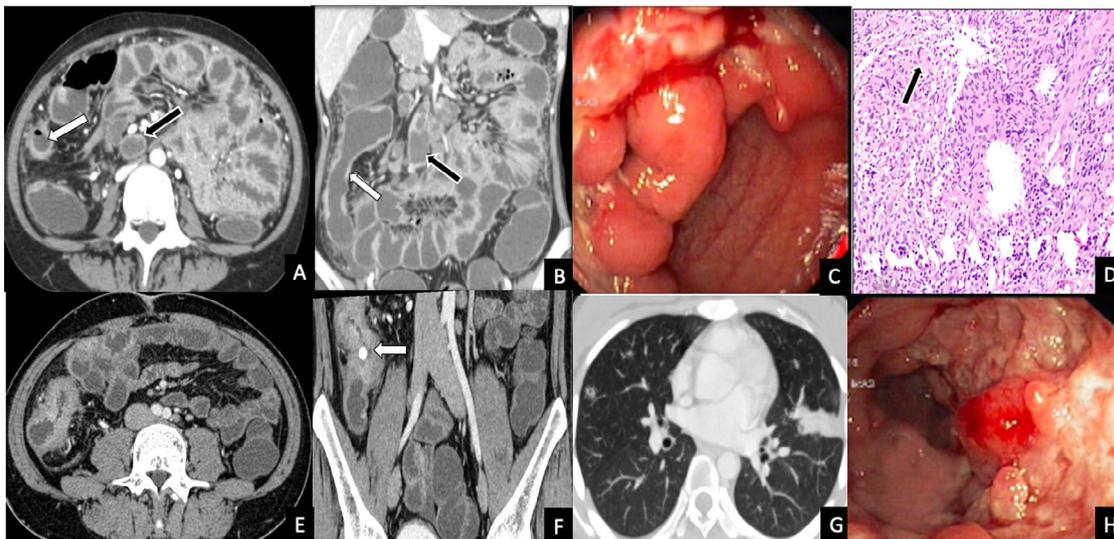


Figure 4 Computed tomography enterography of a 54-year-old man with final diagnosis of intestinal tuberculosis (ITB) (a–d). Axial (a) and coronal (b) images show homogenous bowel wall thickening involving caecum (white arrow in a and b) and necrotic mesenteric lymph nodes (black arrow in a & b); ileocolonoscopy (c) shows polypoid ulceronodular mucosa in cecum; histopathology (d) reveals ileal granuloma with Langhans giant cells (black arrow). Another 43-year-old lady with final diagnosis of ITB (e–h). Axial (e) and coronal (f) images show homogenous bowel wall thickening of terminal ileum with an enterolith (arrow in f) on the coronal image (f); lung window of chest computed tomography (g) shows a focal patch of consolidation in left lung; ileocolonoscopy (d) shows ulceronodular mucosa at terminal ileum.

Table 5 Patient demographics and computed tomography enteroclysis/enterography (CTE) findings in Crohn's disease and intestinal tuberculosis patients

Parameter	Intestinal tuberculosis (<i>n</i> = 61)	Crohn's disease (<i>n</i> = 24)	<i>P</i> *
Age mean ± SD in years	44 ± 12	43 ± 8	—
Gender M: F	35:26	14:10	0.029
CTE:			
Incidence of bowel wall thickening	55/61 (90.2%)	22/24 (91.6%)	0.831
Long-segment bowel involvement	15 (24.6%)	10 (41.7%)	0.119
Short-segment bowel involvement	40 (65.6%)	12 (50%)	0.185
Bowel lesions:			
Homogenous pattern	48 (78.7%)	1 (4.2%)	<0.001
SIF pattern	0 (0%)	11 (45.8%)	<0.001
SMH pattern	7 (11.5%)	11 (45.8%)	0.001
Skip lesions	12 (19.7%)	15 (62.5%)	0.001
Stricture	9 (14.7%)	10 (42%)	0.007
Dilatation of bowel loop	4 (6.5%)	5 (20.8%)	0.109
Location of bowel:			
Duodenum	3 (5%)	0 (0%)	0.555
Jejunum	1 (1.6%)	2 (8.3%)	0.191
Ileum	14 (2.3%)	14 (58.3%)	0.002
Confluent involvement	35 (57.4%)	4 (16.7%)	0.001
Large bowel	2 (3.3%)	3 (12.5%)	0.134
Ancillary findings:			
Lymphadenopathy	22 (36%)	5 (20.8%)	0.175
Lymph node with necrosis	17 (28%)	0 (0%)	0.002
Lymph node with calcification	9 (14.8%)	0 (0%)	0.055
Lung findings	24 (39%)	0 (0%)	0.001
Enteroliths	19 (31%)	1 (4.2%)	0.009
Ascites	10 (16.4%)	0 (0%)	0.056
Comb sign	2 (3.3%)	18 (75%)	<0.001
Mesenteric fat stranding	20 (33%)	10 (41.6%)	0.441
Peritoneal thickening	4 (6.6%)	0 (0%)	0.573
Fibrofatty proliferation	0 (0%)	2 (8.3%)	0.077

**P* < 0.05.

SIF, stratification with intervening layer of fat; SMH, stratification with mucosal hyperenhancement.

CTE findings. Other parameters were expressed as numbers and percentages.

Written informed consent was obtained in English or the local language (Hindi) from all patients before undergoing CT enteroclysis and enterography. All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Results

A total of 150 patients underwent CT enteroclysis, and 150 underwent CT enterography. Of all 300 patients, 125 patients in our study did not have any bowel-related disease on CTE or other investigations. Sixty-one patients had a final

diagnosis of ITB, and 24 patients had CD. The distribution of other diseases in the study sample was as follows: 25 patients had strictures of unknown etiology, bowel neoplasms (*n* = 21), ulcerative colitis (*n* = 11), bowel polyps (*n* = 7), nontubercular bowel infections (*n* = 5), subacute appendicitis (*n* = 8), malabsorption (*n* = 5), malrotation (*n* = 5), and duodenal ulcers (*n* = 3) (Table 1). Table 2 shows the mode of diagnosis of patients with CD or ITB based on CTE, endoscopy, histopathology, or response to empirical therapy. Twenty-four patients of ITB underwent 6 months' ATT trial before finally being diagnosed with ITB. Of these, nine patients underwent a repeat endoscopy post-ATT trial, which showed healed ulcer scars, reinforcing the final diagnosis of ITB. The endoscopic follow up was not available for 15 patients; however, telephonic follow up of these patients revealed no relapse of symptoms 12 months after completion of ATT. Five CD patients underwent an ATT trial of 6 months with no symptomatic response, and good clinical response was seen subsequent to CD-specific treatment. A total of 85 patients with a final diagnosis of ITB or CD were included for further analysis.

The incidence of both CD and ITB was more common in the 31–45 years age group. Symptoms of weight loss (75%), fever (73.7%), and loss of appetite (73.7%) were more common in ITB, whereas abdominal pain (79.2%), loose stools (70.8%), and melena (33.3%) were commonly seen in CD (Table 3).

The CTE findings in patients of ITB and CD are summarized in Table 3. The overall sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CTE to detect bowel wall thickening in both ITB and CD were 90.6, 100, 100, and 94% respectively. The sensitivity of CTE (ITB vs CD, 90.2 vs 91.6%) was higher than the sensitivity of ileocolonoscopy (ITB vs CD, 87 vs 83.3%). CTE and ileocolonoscopy showed significant agreement (kappa value = 0.79) with the final diagnosis, and a strong association was seen between the two modalities with the final diagnosis (phi correlation coefficient = 0.81). Table 4 shows a comparison of endoscopy/colonoscopy findings in patients with CD and ITB.

CTE detected bowel wall thickening in 90.2% patients of ITB and 91.6% of CD patients. CTE failed to show bowel lesions in six cases of ITB and two cases of CD, wherein ileocolonoscopy showed small, nonspecific ulcers at the terminal and distal ileum and were subsequently diagnosed as ITB/CD on endoscopic biopsy or demonstrated improvement on empirical therapy. Isolated involvement of ileum was significantly more common in CD than ITB (CD vs ITB, 58.3 vs 2.3%, *P* = 0.002). Confluent bowel involvement of terminal ileum, ileocecal junction, and adjacent colon was significantly more common in ITB compared to CD (57.4 vs 16.7% respectively, *P* = 0.001). The jejunum was more commonly involved in CD than in patients of ITB with no statistical significance (8.3 vs 1.6%, respectively, *P* = 0.191). The long segment of bowel involvement was more commonly seen in CD compared to ITB (41.7 vs 24.6%, respectively), whereas short segment bowel lesions were seen in 50% of CD and 65.5% of ITB patients; however, there was no statistical significance in the long and short segmental involvement (*P* = 0.119 and 0.185, respectively) of the bowel in these two pathologies.

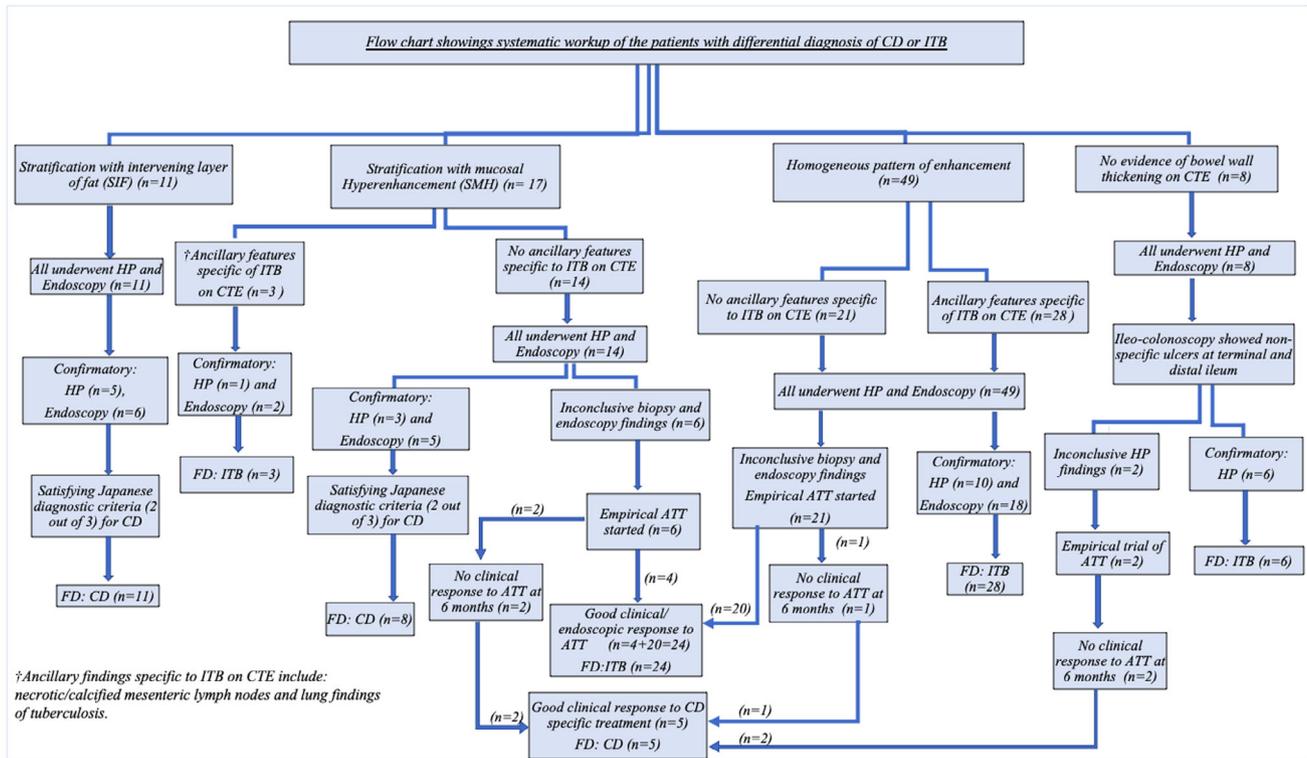


Figure 5 Flow chart showing systematic computed tomography enteroclysis/enterography (CTE) workup of the patients with intestinal tuberculosis (ITB) and Crohn's disease (CD) performed as per case record form. Ancillary findings specific to ITB include: necrotic/calified lymph nodes and lung findings of tuberculosis. ATT, antitubercular therapy; FD, final diagnosis; HP, histopathology.

The homogenous pattern of bowel wall thickening showed no difference in HU value across the inner mucosal to outer serosal layer. In the SIF pattern, the middle hypodense layer had a mean value of -18 HU (range -5 to -40.5 HU). In the SMH pattern, the mucosal hyperenhancing layer had a mean value of 89 HU (range 96 – 126 HU). A homogenous pattern of bowel wall thickening was significantly more common in ITB compared to CD (78.7 vs 4.2% , respectively, $P < 0.001$) (Fig. 1). The SIF pattern of bowel wall thickening (Fig. 2) was found to be specific and significantly associated with patients of CD than ITB (45.8 vs 0% , respectively, $P < 0.001$). The SMH type of thickening was significantly more common in CD compared to ITB (45.8 vs 11.5% , respectively, $P = 0.001$) (Fig. 3).

The necrotic mesenteric lymph nodes had a mean value of 12 HU at the center (range 16 – 27 HU) (Fig. 4). The non-necrotic locoregional lymph nodes had a mean value of 76 HU at the center (range of 45 – 102 HU). Necrotic lymph nodes (28% , $P = 0.002$) and lung findings (39% , $P = 0.001$) were specifically and significantly associated with ITB. Mesenteric lymph nodes with calcification (14.8% , $P = 0.055$), peritoneal thickening (6.6% , $P = 0.573$), and ascites (16.4% , $P = 0.056$) were seen only in patients with ITB without any statistical significance. Other ancillary findings like enteroliths (ITB vs CD, 31 vs 4.2% ; $P = 0.009$) were significantly common in patients of ITB, whereas strictures (ITB vs CD, 14.7 vs 42% ; $P = 0.007$), comb sign (ITB vs CD, 3.3 vs 75% ; $P < 0.001$),

and skip lesions (ITB vs CD, 19.7 vs 62.5% ; $P = 0.001$) were significantly more common in patients with CD (Table 5). The incidence of mesenteric fat stranding was more common in patients of CD than ITB, without any statistical significance (41.6 and 33% , respectively; $P = 0.441$). Fibrofatty proliferation was seen only in CD patients (8.3% , $P = 0.077$) without any statistical significance.

The flow chart showing a summary of the systematic workup in characterizing CTE findings in patients of ITB and CD is summarized in Figure 5.

Discussion

CTE provides a good assessment of the various patterns of bowel wall enhancement and extraluminal information, which are essential to differentiate ITB and CD.¹⁶ Symptomatology plays an important role in differentiating the two diseases and also for assessing responses to empirical therapy.^{1,17,18} In our study, symptoms of fever, weight loss, and loss of appetite were more commonly seen in patients of ITB, whereas loose stools and melena were more commonly seen in patients with CD.

The pattern of bowel wall enhancement provides a leading clue to the diagnosis. Few studies have mentioned that the homogenous pattern of enhancement is commonly seen in ITB and that the mural stratification pattern of bowel wall enhancement is frequently observed in CD.^{19,20} In our study, the patterns

of bowel wall thickening were specifically defined and divided into three types—homogenous pattern, SIF pattern, and SMH pattern. The homogenous pattern of enhancement was significantly more common in ITB, whereas the SIF pattern was significantly and specifically associated with CD. The third pattern of enhancement (SMH) was seen in both ITB and CD with slightly higher predominance in CD. In patients with the SMH pattern, the location of bowel involvement and ancillary findings had a great role in narrowing the differential diagnosis.

On histopathology, the initial lesions in both ITB and CD first involve the mucosa of the bowel.^{18,21,22} Granulomas in ITB are more confluent with lymphoid cuffing and disproportionate amounts of submucosal inflammatory cell infiltrate and may show caseation necrosis; granulomas of CD show a more discrete distribution. Both ITB and CD further progress to show transmural involvement of the bowel wall.^{16,23,24} Radiologically, the initial mucosal involvement in ITB and CD with associated submucosal inflammation may be responsible for the mucosal hyperenhancement and stratification as observed in the SMH pattern on CTE.²⁵ Progression of ITB and CD to transmural involvement may be the reason for homogenous bowel wall enhancement on CTE.^{17,20} Submucosal fat deposition is a frequently observed finding in CD, the pathogenesis of which is uncertain.^{26,27} Submucosal fat deposition is responsible for the SIF pattern of bowel wall enhancement observed in CD. Amitai *et al.*,²⁸ in a study of 100 patients with CD, have mentioned that submucosal fat was seen in 17% of patients and that the middle hypodense layer of fat had a mean value of -26 HU. In our study, the SIF pattern was seen in 45.8% of CD patients, who were not previously diagnosed cases and presented to our hospital with active symptomatology. The middle hypodense layer in the SIF pattern had a mean value of -18 HU. Cheng *et al.*²⁵ concluded that the bowel wall thickening, degree of mural stratification, and enhancement on CTE were potential visual biomarkers to access CD disease activity. They also mentioned that the hyperenhancing mucosa had CTE values ranging between 80 and 89.2 HU in moderate to severe CD. In this study, 58.9% of CD patients had the SMH pattern, and the hyperenhancing mucosal layer had a mean value of 89 HU. Choi *et al.*²⁰ defined four patterns of bowel enhancement and found that the stratified patterns of enhancement were associated with active CD and that the homogenous pattern of bowel thickening was associated with disease remission. We found that only 4.2% patients of CD in our study had a homogenous pattern of enhancement, and they had active symptoms of CD with multiple aphthous ulcers on endoscopy at the terminal ileum.

ITB has a predilection for contiguous bowel involvement, especially the terminal ileum and ICJ.^{7,16,19,29} In our study, confluent bowel involvement was significantly more common with ITB, whereas isolated ileal thickening was significantly more common in CD. The involvement of duodenum, jejunum, or large bowel as a location-specific site and long or short length of bowel involvement did not show any statistically significant association with either of the diseases. In this study, ancillary features like lung changes (centrilobular nodules/tree in bud infiltrates) and necrotic and calcified mesenteric lymph nodes were specific for ITB, whereas comb sign, mesenteric changes (mesenteric fat stranding, fibrofatty proliferation), and skip lesions were commonly seen in CD.^{15,18,30-32} Ascites and peritoneal

Table 6 Comparison of incidence of associated extraintestinal findings between Crohn's disease and intestinal tuberculosis

	Present study			Park <i>et al.</i>			Kedia <i>et al.</i>			Zhang <i>et al.</i>			Mao <i>et al.</i>		
	ITB	CD	P*	ITB	CD	P	ITB	CD	P	ITB	CD	P	ITB	CD	P
Ascites	16.4%	0%	0.012	27.3%	20.4%	0.691	—	—	—	29%	—	—	—	—	—
Comb sign	3.3%	75%	0.009	9.1%	74.1%	0.001	20%	44.45%	0.01	32.3%	7.6%	0.002	7.9%	80.6%	0.001
Cocoon formation	1.6%	0%	0.326	—	—	—	—	—	—	—	—	—	—	—	—
Enteroliths	31%	4.2%	0.002	—	—	—	—	—	—	—	—	—	—	—	—
Lymphadenopathy	36%	20.8%	0.232	27.3%	53.7%	—	20%	1.9%	<0.01	—	—	—	—	—	—
Lymph node with necrosis	28%	0%	0.004	9.1%	0%	0.169	—	—	—	35.5%	0%	0.001	28.9%	0%	<0.001
Lymph node with calcification	14.8%	0%	0.055	9.1%	0%	0.169	—	—	—	6.5%	0%	0.018	28.9%	0%	<0.001
Lung changes	39%	0%	0.001	—	—	—	—	—	—	—	—	—	—	—	—
Mesenteric fat stranding	33%	41.6%	0.441	—	—	—	20%	13%	0.33	0%	14.1%	0.018	39.5%	52.2%	0.208
Peritoneal thickening	6.6%	0%	0.573	0%	0%	—	—	—	—	—	—	—	—	—	—
Fibro-fatty proliferation	0%	8.3%	0.077	9.1%	46.3%	0.039	12%	18.5%	0.36	—	—	—	5.3%	37.3%	<0.001

*P < 0.05.

CD, Crohn's disease; ITB, intestinal tuberculosis.

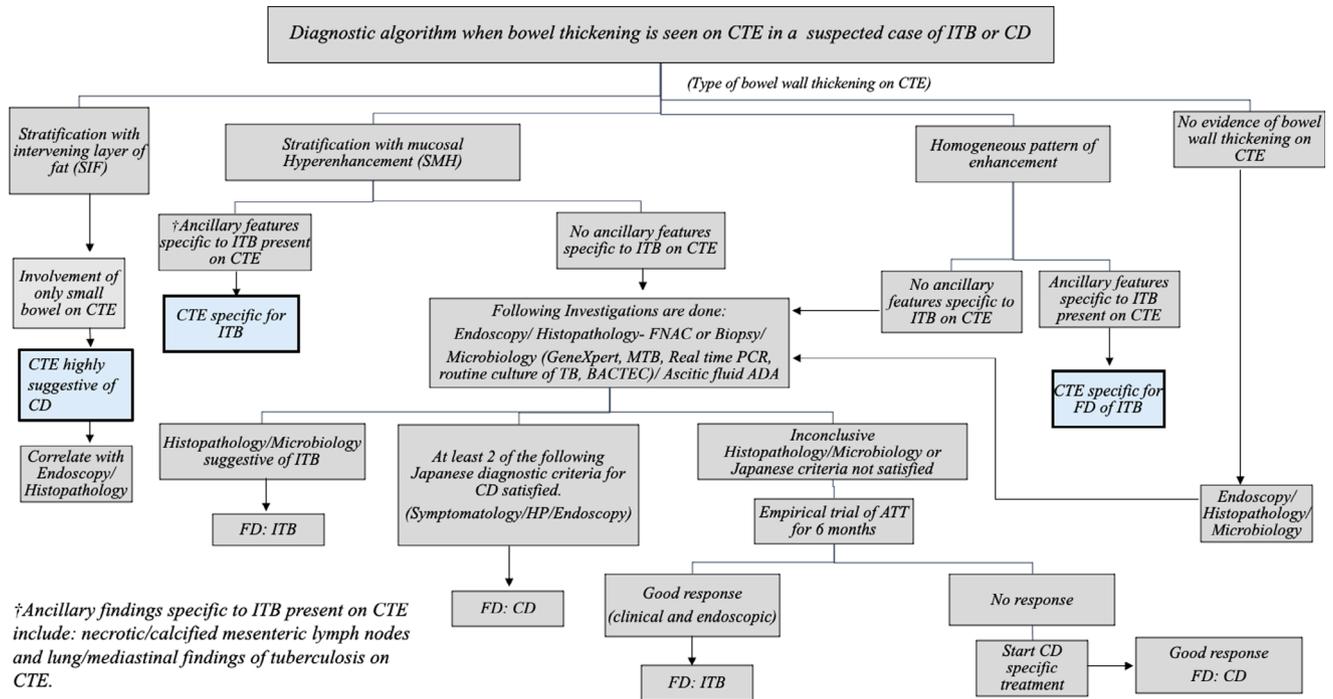


Figure 6 Proposed diagnostic algorithm for a suspected case of intestinal tuberculosis (ITB) or Crohn's disease (CD) undergoing computed tomography enteroclysis/enterography (CTE). ADA, Adenosine deaminase; ATT, antitubercular therapy; FD, final diagnosis.

thickening are ancillary features that favor ITB, also observed in our study.^{7,15} A comparison of incidences of extraintestinal CTE findings of ITB and CD in our study and other recent studies is listed in Table 6.

The sensitivity of CTE to detect the bowel lesions is higher than that of ileocolonoscopy as the former not only demonstrates the extraintestinal findings but also permits complete evaluation of all bowel segments.^{33–37} In our study, the sensitivity of diagnosing ITB/CD increased from 90.6 to 97.7% by combining findings on CTE with ileocolonoscopy, suggesting that all mucosal abnormalities cannot be delineated on CTE, and a combination of these two modalities increases the sensitivity of diagnosis.

We have attempted to define objective criteria based on HU values for categorizing patterns of bowel wall enhancement and defining lymph nodes as necrotic or nonnecrotic. This will avoid any future interobserver variation while reporting on a standard format. An algorithmic approach for patients undergoing CTE with suspected ITB/CD has been suggested by us (Fig. 6). Although our study shows that the differentiation between ITB and CD can be made by combining symptomatology/CTE/endoscopy/HP/microbiology, there are a few limitations. The final diagnosis of bowel lesions in 8.3% patients with strictures of unknown etiology could not be ascertained during the study period and were excluded from the analysis. A relatively smaller population of CD patients in this sample may be another limiting factor. It has also been observed that nearly 38% patients of CD show global response to ATT; however, no mucosal healing is seen at follow-up endoscopy. The likely reason suggested is that there may be mycobacterium paratuberculosis

infection in CD patients or probably because both ITB and CD are Paneth cell diseases.³⁸ In our study, 9 of 24 patients in an empirical ATT trial underwent repeat endoscopy, which showed mucosal healing. However, endoscopic follow up was not possible in 15 patients, although these patients did not have relapse of symptoms after 12 months of completion of ATT. We believe that a repeat endoscopy would have reinforced this diagnosis.

In conclusion, CTE can resolve the dilemma of ITB and CD to a great extent with the help of enhancement pattern of bowel lesions and specific ancillary CTE findings. The SIF pattern on CTE with small bowel involvement is highly suggestive of CD. Bowel lesions with associated necrotic and calcified mesenteric lymph nodes are specific for ITB. By forming objective criteria and with the help of format-based reporting, the various interobserver variations can be reduced, and radiologists can arrive at a more confident diagnosis.

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