ORIGINAL ARTICLE

Etiology of isolated terminal ileal ulcers in symptomatic patients

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ABSTRACT

Introduction: Isolated terminal ileal ulcers (ITIUs) are being frequently encountered by the clinicians with the increasing numbers of ileal intubation during colonoscopies. This study was aimed at finding the etiologies of these ulcers in symptomatic patients and their association with various clinical features.

Methods: This was a hospital based prospective, observational, descriptive study performed on all consecutive patients who underwent ileocolonoscopy for various gastrointestinal symptoms between 1 July 2018 and 30 June 2019. Clinical, endoscopic and histopathological findings were analyzed to determine the etiology of ITIUs in symptomatic patients. Statistical analysis was done by SPSS 20.

Results: Among 60 (7.67%) of 782 symptomatic patients who had ITIUs on ileocolonoscopy, specific etiologies were established in 28 (46.67%) of them. Intestinal TB was the most common specific diagnosis, which was seen in 18 (30%) patients. Chronic abdominal pain with or without chronic diarrhea was the most common indication for ileocolonoscopy.

Conclusions: Specific etiologies like tuberculosis, Crohn's disease, NSAID-induced ulcer and intestinal spirochetosis were seen in 28 (46.67%) of patients with isolated terminal ileal ulcers. The most common clinical features were chronic abdominal pain (65%) and abdominal pain with diarrhea (16.7%). No clinical presentation was significantly associated with any specific etiology, thus emphasizing the need for routine ileal intubation and tissue sampling for histopathological examination in all symptomatic patients undergoing colonoscopy.

Key words: *Colonoscopy; crohn's disease; intestinal tuberculosis; Isolated terminal ileal ulcer.*

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INTRODUCTION

With an increasing number of ileal intubations during colonoscopy, it is not uncommon to detect single or multiple ulcers in terminal ileum.[i] The diagnosis of specific cause of ileitis is important, because misdiagnosis may result in delays or errors in patient management.[ii]

Isolated terminal iliac ulcer (ITIU) is defined as chronic inflammation of the terminal ileum, manifesting as superficial or deep terminal ileal ulcers without involving ileocecal valve or colonic mucosa. The most frequent specific diagnosis obtained by ileoscopy has been Crohn's disease (CD) in previous studies. [iii , iv] Although ITIUs are frequently diagnosed during colonoscopic procedures, no study has been carried out in Nepal regarding possible etiology. Thus, a major gap exists regarding the knowledge of etiology, natural course and clinical significance of ITIU.

The present study aimed at studying the etiology of ITIUs detected on ileocolonoscopy in patients with gastrointestinal symptoms at a tertiary care center in Nepal.

METHODS

This single-centered prospective, observational, descriptive study was performed by evaluating all the patients undergoing ileocolonoscopy for gastrointestinal symptoms at the Gastroenterology unit of National Academy of Medical Sciences (NAMS), Bir Hospital, Kathmandu, Nepal from 1 July 2018 to 30 June 2019. Patients who showed single or multiple ITIUs as the sole endoscopic abnormality were recruited. Patients who refused to consent, had incomplete colonoscopy (due to colonic strictures or growths) and those with colonic or ileocecal ulcers were excluded from the study.

The study protocol was approved by the Institutional Review Board (IRB), NAMS. For recruited patients, demographic data, clinical features, history of NSAID intake, colonoscopic and histological findings were noted. Colonoscopy was done by the gastroenterologists at Gastroenterology unit of Bir Hospital with video colonoscopes (Fujinon and Pentax) without sedation, after preparation with polyethylene glycol electrolyte lavage solution. The withdrawal time of the colonoscope was not less than 6 minutes in all the patients. In patients with ITIUs, biopsies were taken from the ulcer margins and base, and sent in formalin for histopathology. The final diagnosis was based on histopathology. Categorical variables are compared using chi square or Fischer's exact whichever was applicable. Quantitative variables were compared using independent student's t test. P value of <0.05 are considered to be statistically significant. SPSS software version 20 was used for data analysis.

RESULTS

A total of 822 colonoscopies were performed for various indications between 1 July 2018 and 30 June 2019. Colonoscopy could not be completed in 18 patients (2.19%) due to various reasons like strictures, malignancies or difficult anatomy. Ileal intubation was successful in 782 patients out of 804 completed colonoscopies (97.26%). ITIUs were seen in 60 patients out of 782 ileocolonoscopies (7.67%). Specific etiologies like tuberculosis, Crohn's disease, NSAID-induced ulcer and intestinal spirochetosis were established in 28 (46.67%) of patients with ITIUs.

The demographic details, clinical presentations, colonoscopic findings and histologic diagnosis are summarized in Table 1. The mean age of the study population was 44.78±14.51 years, and 44 out of 60 patients (73.3%) were males. The most common indications for colonoscopy were chronic

abdominal pain (65%) and abdominal pain with diarrhea (16.7%). Other indications are shown in Table 2. The symptoms of anorexia, weight loss and fever were significantly associated with a specific diagnosis (P= 0.00). The pattern of distribution of other symptoms was not statistically significant (Table 3). The number of ulcers was not significantly associated with any etiology.

Determining the etiology of ITIUs on the basis of colonoscopic findings was not possible. Solitary ileal ulcer was present in 15 (25%) patients and multiple ulcers were present in 45 (75%) patients. However, 83.3% (15 out of 18) of patients with TB and 80% (four out of five) of patients with Crohn's disease had multiple ulcers.

A subgroup analysis among patients diagnosed with Crohn's disease and TB was done to evaluate their association between the indications and findings of colonoscopy, as shown in Table 4. It was shown that the presence of anorexia and fever were significantly associated with TB. No other presentation was significantly associated with either of the diagnoses. None of the colonoscopic finding was associated with any of the two diseases.

Table 1. The demographic details, clinical presentations, colonoscopic findings and histologic diagnosis

	Normal (N=5)	Non-specific ileitis (N=27)	Crohn's disease (N=5)	TB (N= 18)	Intestinal spirochetosis (N= 1)	NSAID induced ulcer (N=4)	P value
Demographics							
Gender (M/ F)	1/ 4	21/ 6	5/ 0	14/ 4	1/ 0	2/ 2	
Age	51.80±3.63	43.48±14.11	46.40±13.88	38.28±13.22	65.00	67.00±2.00	0.00[a]
Clinical presentations							
Pain abdomen	3 (60%)	25(92.6%)	5 (100%)	17 (94.4%)	1 (100%)	4 (100%)	0.17[b]
Diarrhea	0 (%)	8 (29.6%)	1 (20%)	7 (38.9%)	0 (0%)	0 (0%)	0.38[b]
Anorexia	2 (40%)	13 (48.1%)	0 (0%)	17 (94.4%)	0 (0%)	0 (0%)	0.00[b]
Vomiting	0 (%)	0 (0%)	0 (0%)	4 (22.2%)	0 (0%)	0 (0%)	0.07[b]
Fever	0 (%)	1 (3.7%)	0 (0%)	12 (66.67%)	1 (100%)	0 (0%)	0.00[b]
Weight loss	0 (%)	10 (37.00%)	5 (100%)	16 (88.9%)	0 (0%)	0 (0%)	0.00[b]
Colonoscopic findings							
Solitary ulcer (N= 15)	2 (40%)	8 (29.6%)	1 (20%)	3 (16.7%)	1 (100%)	0 (0%)	
Multiple ulcers (N= 45)	3 (60%)	19 (70.4%)	4 (80%)	15 (83.3%)	0 (0%)	4 (100%)	0.31[b]

[a]Student t-test, [b]Fisher's exact test, TB:Tuberculosis, NSAID:Non-steroidal anti-inflammatory drug

Table 2. Indications for colonoscopy

Indications	Frequency N (%)
Abdominal pain	39 (65%)
Abdominal pain with chronic diarrhea	10 (16.7%)
Abdominal discomfort	6 (10%)
Chronic diarrhea	2 (3.3%)
Blood-mixed stool	2 (3.3%)
Abdominal distension	1 (1.7%)
Total	60 (100%)

Table 3. Positive rates of significant histopathology according to indications for colonoscopy

Variable	Specific Diagnosis	Non-specific Diagnosis	P value
Abdominal pain	27 (49.10%)	28 (50.90%)	0.35*
Chronic diarrhea	8 (50%)	8 (50%)	0.78
Weight loss	21 (67.7%)	10 (32.3%)	0.00
Anorexia	17 (53.1%)	15 (46.9%)	0.28
Vomiting	4 (100%)	0 (0.00%)	0.04*
Fever	13 (92.9%)	1 (7.1%)	0.00

* Fisher's exact test

Table 4. Subgroup analysis for association of clinical features and colonoscopic findings with Crohn's disease and Tuberculosis

Variable	Crohn's Disease (N= 5)	Tuberculosis (N= 18)	P value
Gender (M/F)	5/0	14/4	0.54*
Age	46.4±13.89	38.28±13.22	0.24**
Abdominal pain	5 (100%)	17 (94.4%)	1.00*
Chronic diarrhea	1 (20%)	7 (38.9%)	0.62*
Weight loss	5 (100%)	16 (88.9%)	1.00*
Anorexia	0 (0%)	17 (94.4%)	0.00*
Vomiting	0 (0%)	4 (22.20%)	0.54*
Fever	0 (0%)	12 (66.70%)	0.01*
Colonoscopy			
Solitary ulcer	1 (20%)	3 (16.70%)	1.00*
Multiple ulcers	4 (80%)	15 (83.3%)	

*Fisher's exact test
**Student t-test

DISCUSSION

There are a few studies that have described the clinical course and follow up of asymptomatic terminal ileitis.[v] But the data on symptomatic ITIUs is limited. No study has been carried out on terminal ileal ulcers in Nepal. This study was carried out to understand the etiology of ITIUs in patients presenting with gastroenterology symptoms. It was found that 60 out of 782 (7.67%) patients who underwent ileocolonoscopy had ITIUs. In a study done by Kedia S, et al. [vi] in India, ITIUs were present in 7% of 898 patients undergoing ileocolonoscopy, which was similar to our finding.

Specific etiologies could be established in 28 (46.67%) patients with ITIUs. The final diagnoses that could be ascertained were TB: 18 (30.00%), Crohn's disease: Five (8.33%), NSAID-induced ileal ulcer: Four (6.67%), intestinal spirochetosis: One (1.67%). Non-specific ileitis was seen in 27 (45%) patients. Histopathology was normal in five (8.33%) patients. None of the patients with gastrointestinal symptoms and ITIUs had malignancies, lymphomas or vasculitis. Mehta V, et al.[2] had recently performed a study on symptomatic ITIUs, in which 4.9% of 1497 patients who underwent ileocolonoscopy had ITIUs. They could ascertain the final diagnosis among 44 (59.5%) of the ITIU patients. Contrary to our study, where intestinal TB was the most common diagnosis (30% of total ITIUs), their study had CD as the most common final diagnosis (25.7% of total

ITIUs). We did not follow up our patients, whichcould have missed the diagnosis in at least a few of them.

Abdominal pain with or without chronic diarrhea was the most common symptom, irrespective of the final diagnosis. Other symptoms that were not associated with any diagnosis were anorexia, vomiting, blood-mixed stool, abdominal discomfort/distension. Fever was significantly associated with TB, whereas patients with CD and TB were associated with weight loss. Although these findings were similar to a recent study from India[3], weight loss was not associated with any diagnosis in their study.

On ileoscopy, there was no significant difference in appearance of the ulcers between different etiologies, although most of the ulcers in TB (83.33%) and CD (80%) were multiple, though statistically not significant. This finding was similar to the study of Mehta V, et al.[2] The most frequent specific diagnosis for ITIUs in our study was intestinal TB, which could be due to the high prevalence of pulmonary TB in our country. However, this finding was different from other studies on ITIUs, where CD was found to be the most common specific diagnosis.[2,3,] [vii] However, in a country like Nepal where TB is highly prevalent, the diagnosis of ITIU may pose a clinical dilemma, because differentiating CD from TB is very important on one hand and very challenging on the other. Patients might be subjected to lifelong and potentially harmful treatments if their condition is misdiagnosed. The natural history of patients with ITIUs has not been well described. It is important to differentiate between patients who require a further evaluation to rule out intestinal tuberculosis (ITB) or Crohn's disease (CD) and those who can just be followed up symptomatically.[6]

Normal histology was seen in five (8.33%) patients with ITIUs. This could be because of the use of polyethylene glycol for colonic lavage, which can cause aphthous ulcers in the intestines. However, such ulcers are more common with the use of sodium phosphate bowel preparation than with polyethylene glycol.[viii]

Intestinal spirochetosis (IS) was seen inone patient with ITIUs. This patient was a 65 year old immunocompetent gentleman who had presented with pain abdomen for six weeks and fever for five days. Ileocolonoscopy had revealed a solitary ITIU. Human IS is a condition defined histologically by the presence of spirochetal microorganisms attached to the apical cell membrane of the colorectal epithelium. Intestinal spirochetes comprise a heterogeneous group of bacteria. [ix] Symptomatic IS is most commonly accompanied by complaints of chronic (watery) diarrhea and vague abdominal pain without other apparent cause.[x] Only a few human cases on this condition, especially among immunocompetent individuals, have been reported. In a recent case series oftwo young immunocompetent male patients from Canada with chronic pain abdomen and loose bowel movements reported by Gozdzik M, et al., both the cases were diagnosed by histopathology. Both were treated with a 10 days course of oral metronidazole with improvement of

symptoms and clearance of bacteria on repeat biopsy.[xi]

The limitations of this study include its small sample size, thus preventing us from carrying out a multivariate analysis of the symptom profile to predict a diagnosis of ITIUs. Supportive tests like tissue TB-PCR and fecal calprotectin were not used, which would have helped in diagnosing intestinal TB or CD. Patients were not followed up. Had we been able to follow up the patients, we could probably have identified more patients with specific diagnosis.

CONCLUSION

Specific etiologies like tuberculosis, Crohn's disease, NSAID-induced ulcer and intestinal spirochetosis were seen in 28 (46.67%) of patients with isolated terminal ileal ulcers. The most common clinical features were chronic abdominal pain (65%) and abdominal pain with diarrhea (16.7%). No clinical presentation was significantly associated with any specific etiology, thus emphasizing the need for routine ileal intubation and tissue sampling for histopathological examination in all symptomatic patients undergoing colonoscopy.

CONFLICT OF INTEREST

None

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None

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