

# Conformity between Ileoscopy Appearance with Terminal Ileum Histopathology Appearance in Normal Colonoscopy Chronic Diarrhea Patients

Indra Marki\*, Ari Fahrial Syam\*\*, Irsan Hasan\*\*\*

\* Department of Internal Medicine, Mitra Kelapa Gading Hospital, Jakarta

\*\* Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, University of Indonesia/Dr.Cipto Mangunkusumo General National Hospital, Jakarta

\*\*\* Division of Hepatology, Department of Internal Medicine, Faculty of Medicine, University of Indonesia/Dr.Cipto Mangunkusumo General National, Jakarta

## ABSTRACT

**Background:** Chronic diarrhea is one of the most common problem in gastroenterology cases. Ileoscopy is one of the modalities to determine the etiology of chronic diarrhea by normal colonoscopy appearance. Recently, there is still controversy in the need of this examination in normal macroscopic appearance. The aim of this study is to study the conformity of histopathology abnormalities with ileoscopy appearance in chronic diarrhea patients with normal colonoscopy.

**Method:** This study uses cross sectional study design by collecting 60 medical record data in several hospitals in Jakarta in the period of 1 January 2005 to 31 December 2011. Diagnostic test between ileoscopy and histopathology is performed by histopathology examination as a gold standard.

**Results:** Study results revealed conformity between both examinations for 93.33%. Sensitivity value of ileoscopy examination compared to histopathology as a gold standard was 94%, specificity 90%, positive predictive value 97.9%, and negative predictive value 75%.

**Conclusion:** Ileoscopy examination in chronic diarrhea patients and normal colonoscopy showed similar results with histopathology examination.

**Keywords:** ileoscopy, histopathology, conformity, chronic diarrhea

## ABSTRAK

**Latar belakang:** Diare kronik merupakan salah satu masalah yang sering dijumpai pada kasus gastroenterologi. Ileoskopi merupakan salah satu modalitas untuk menegakkan etiologi diare kronik dengan gambaran kolonoskopi yang normal. Sampai saat ini masih terdapat kontroversi mengenai perlunya pemeriksaan tersebut pada gambaran makroskopik yang normal. Tujuan dari penelitian ini adalah untuk mempelajari kesesuaian kelainan histopatologis dengan gambaran ileoskopi pada pasien diare kronik dengan kolonoskopi normal.

**Metode:** Penelitian menggunakan desain studi potong lintang dengan mengumpulkan data rekam medis sejumlah 60 pasien pada beberapa rumah sakit di Jakarta selama periode 1 Januari 2005 sampai 31 Desember 2011. Uji diagnostik antara pemeriksaan ileoskopi dan histopatologi dilakukan dengan pemeriksaan histopatologi sebagai standar baku emas.

**Hasil:** Hasil penelitian menunjukkan kesesuaian antara kedua pemeriksaan tersebut sebesar 93,33%. Nilai sensitivitas pemeriksaan ileoskopi dibandingkan dengan histopatologi sebagai standar baku emas sebesar 94%, spesifisitas 90%, nilai prediksi positif 97,9%, dan nilai prediksi negatif sebesar 75%.

**Simpulan:** Pemeriksaan ileoskopi pada pasien dengan diare kronik dan kolonoskopi normal menunjukkan hasil yang serupa dengan pemeriksaan histopatologi.

**Kata kunci:** ileoskopi, histopatologi, kesesuaian, diare kronik

## INTRODUCTION

Chronic diarrhea is one of the most common problems in gastroenterology cases.<sup>1,2</sup> Patients who suffer from chronic diarrhea will experience disturbance in their quality of life, thus this case need to be managed completely. In western countries the prevalence was 4-5% in general population and 7-14% in elderly patients.<sup>2,3</sup> In Indonesia itself, there has no comprehensive data on the prevalence of chronic diarrhea. However, in a study on morbidity in North Jakarta revealed the prevalence of chronic diarrhea was 1% from all diarrhea cases.<sup>4</sup>

Colonoscopy is one of the modalities in searching for the etiology of chronic diarrhea. In routine examination, macroscopic examination in the every part of the colon was performed, and also biopsy sample was taken to be examined through histology. In cases where colonoscopy revealed normal results, additional ileoscopy examination was performed to establish the diagnosis. Various abnormalities which may be found in terminal ileum include inflammatory bowel disease, *microscopic colitis*, and infection.<sup>5-7</sup> Similar to colonoscopy, in ileoscopy examination, it is also suggested to take tissue sample if we found abnormalities in macroscopic appearance. From studies, it was obtained that terminal ileum histopathological abnormalities are correlated with the macroscopic abnormality.<sup>8,9,10</sup> This is in concordance with the study by Melo et al which stated that conformity between terminal ileum macroscopic appearance with its microscopic appearance reached up to 99.1%.<sup>5</sup> However, there was controversy in the need of histopathology examination from the biopsy of terminal ileum in normal ileoscopy appearance.<sup>5</sup> Misra et al evaluated 50 patients with suspected intestinal tuberculosis and normal ileoscopy, and found only 2 patients with non-caseating granuloma abnormality in histopathology examination.<sup>11</sup> Other studies also stated similar results.<sup>3,6</sup> While on the other hand, several studies reported that evaluation of histopathology in ileum mucosa with normal ileoscopy appearance may give significant hint regarding early pathology process.<sup>10</sup>

Study regarding this matter is very rare worldwide, and also in contrast with one another. Additionally, the results of the study cannot be directly implemented in Indonesia because of various different condition and patients' characteristic, moreover study on this matter is not yet available in Indonesia. In regard to this, we conducted an initial study in Indonesia regarding the need of routine terminal ileum histopathology

examination in chronic diarrhea cases with normal colonoscopy appearance.

## METHOD

This study uses cross-sectional study with target population of the study is patients who were admitted to several hospital in Jakarta during January 2005 to December 2011. Patients' data were obtained from medical records, in the form of general data (age, gender, complaints) and clinical (disease distribution, colonoscopy results, and histopathology). Samples needed were 60 patients by recruiting all chronic diarrhea cases with normal colonoscopy which were listed in the medical record data.

Inclusion criteria in this study are: 1) all chronic diarrhea patients who have undergo colonoscopy, ileoscopy, and terminal ileum histopathology listed in Division of Gastroenterology, Department of Internal Medicine, Cipto Mangunkusumo Hospital and other private hospitals, who were diagnosed for the first time on 1 January 2005 to 31 December 2011; 2) those chronic diarrhea patients have medical record in Cipto Mangunkusumo Hospital and other private designated hospitals; 3) those patients gave normal colonoscopy results, based on criteria. While exclusion criteria was patients with abnormal colonoscopy results.

From the collected data, data completeness and data cleaning were evaluated. Data were further tabulated, given code, and inserted into the computer. Data analysis were performed using programme SPSS 17. Collected data were analysed using diagnostic to determine sensitivity, specificity, positive predictive value, and negative predictive value.

## RESULTS

Based on the obtained data, total patients were 60 patients, with number of males and females were 30 patients each. Most patients were at the age of 31-50 year old was 45%. Most tribe were Javanese, which were 50%. In this study, it was also obtained that 3 most common accompanying complaints were abdominal pain (25%), followed by hemochezia (15%) and bloating (13.33%). The most common disease to be found is Crohn's disease in 55% patients.

Based on the data, it was obtained that in chronic diarrhea patients with normal colonoscopy, there was 80% abnormal ileum. While in histopathology examination, there was 83.33% abnormal ileum appearance.

**Table 1. Characteristic of chronic diarrhea patients with normal colonoscopy**

Characteristics	Total n (%)
Sex	
Male	30 (50%)
Female	30 (50 %)
Age (years)	
≤ 30	9 (15 %)
31-50	27 (45 %)
≥ 51	24 (40 %)
Complaint other than diarrhea	
Abdominal pain	15 (25%)
Hematochezia	9 (15%)
Bloating	8 (13.33%)
Weight loss	2 (3.33%)
Nausea	2 (3.33%)
Stomatitis	1 (1.67%)
Constipation	1 (1.67%)
No complaints	22 (36.67 %)
Distribution of disease	
Ileitis	13 (21.7 %)
Crohn's disease	33 (55 %)
Typhoid	3 (5 %)
Normal	11 (18.3 %)

**Table 2. Proportions of normal and abnormal ileum based on results of ileoscopy and histopathology examinations in chronic diarrhea with normal colonoscopy**

Ileoscopy	Total n (%)	Histopathology	Total n (%)
Normal	12 (20%)	Normal	10 (16.67%)
Abnormal	48 (80%)	Abnormal	50 (83.33%)
Total	60 (100%)	Total	60 (100%)

In this study, it was found that from 12 subjects with normal ileoscopy appearance, 9 (75%) were concluded to not having significant abnormality. While from 48 abnormal ileoscopy appearance, there was normal result in 1 (2.1%) patient.

Based on the table, it was found that in all normal ileum microscopic examination, there was no significant abnormality being found (histopathology). And in the examination of ileum microscopic examination with abnormality, 1 (2%) was normal.

**Table 5. Diagnostic test ileoscopy compared to histopathology in chronic diarrhea patients with normal colonoscopy**

Ileoscopy	Histopathology		Total
	Abnormal	Normal	
Abnormal	47	1	48
Normal	3	9	12
Total	50	10	60

Conformity between ileoscopy and histopathology examination results found 9 subjects with normal results and 47 subjects with abnormalities. Sensitivity, specificity, and positive predictive value of ileoscopy examinations in detecting ileum abnormality were 94%, 90%, and 97.9%, respectively.

## DISCUSSION

In this study, the number of subjects included were 60 patients with various background. The number of males and females were same, which were 30 patients in each group. The average age of patients was 45.81 year old with the range of 18-77 year old. The largest age group was 31-50 years old which was 27 people. Least patients were found in the age group of below 30 years old. This description is slightly different with other studies, such as study by McHugg et al, in which male were 40% and female were 60%, and the age range was 1- 88 years old.<sup>9</sup> Or in the study by Cherian et al, in which the ratio of male and female was 4.3 and 5.7 and the age range was 8-95 year old.<sup>10</sup>

The most common accompanying complaints beside diarrhea was abdominal pain in 25% subjects, followed by hematochezia in 15% subjects, and bloating in 13.3% subjects. Other documented complaints include weight loss, nausea, stomatitis, and constipation. In studies by Jeong et al and Morini et al found that ileoscopy abnormalities were found particularly in patients with diarrhea and abdominal pain.<sup>12,13</sup>

In this study, abdominal pain and bloating are most commonly found in Crohn's disease. Abdominal

**Table 3. Distribution of diagnosis based on ileoscopy in chronic diarrhea patients with normal colonoscopy**

Ileoscopy	Diagnosis					Total
	Normal	Ileitis	Crohn	Typhoid	Melanosis Coli	
Normal	9 (75%)	1 (8.3%)	1 (8.3%)	0 (0%)	1 (8.3%)	12 (100%)
Abnormal	1 (2.1%)	12 (25%)	32 (66.7%)	3 (6.3%)	0 (0%)	48 (100%)
Total	10 (16.7%)	13 (21.7%)	33 (55%)	3 (5%)	9 (1.7%)	60 (100%)

**Table 4. Distribution of diagnosis based on histopathology in chronic diarrhea patients with normal colonoscopy**

Histopathology	Diagnosis				Total
	Normal	Ileitis	Crohn	Typhoid	
Normal	10 (100%)	0 (0%)	0 (0%)	0 (0%)	10 (100%)
Abnormal	1 (2%)	13 (26%)	33 (66%)	3 (6%)	50 (100%)
Total	11 (18.3%)	13 (21.7%)	33 (55%)	3 (5%)	60 (100%)

pain in 28.12% patients with Crohn's disease, and bloating in 15.6% patients. Therefore, it is expected that clinicians are able to increase their awareness in facing diarrhea cases which is followed by abdominal pain and bloating.

This study described results of ileoscopy and histopathology examinations. It is seen that if using histopathology examination as a gold standard, ileoscopy examination has sensitivity of 94%, which means that if there was abnormality in histopathology examination, then the possibility of ileoscopy examination to exhibit similar results was 94%. The specificity of ileoscopy was 90%, which means that if histopathology examination did not found any abnormality, then the possibility of ileoscopy examination to show normal results was also 90%. Meanwhile, the positive predictive value was 97.9%, which means that if the results were positive, then 97.9% of the results of this test will show real positive results. These illustrated that ileoscopy examination was almost similar to histopathology in detecting the presence of abnormality in the ileum. This was in concordance with the study performed in Canada, where in detecting Crohn's disease, the sensitivity of ileoscopy was 92.9% and the specificity was 100%.<sup>14</sup>

From twelve patients with normal ileoscopy, 3 of them had histopathology abnormalities. In 1 patient, the results of examination was beneficial to establish diagnosis. The histopathology abnormalities found in this study include ileitis (1 case), melanosis coli (1 case), and ileitis in line with Crohn (1 case). Therefore this suggested that in normal ileoscopy appearance, there can be histology abnormalities 25%, where only 1 (8.3%) patient was able to gain diagnosis. This was almost similar to other studies, where in normal ileoscopy examination, abnormalities found were only about 0–16.5%.<sup>10,13,15</sup>

With obtained abnormality value was only 8.3% of all subjects with normal mucosa, this described that histopathology examination was not needed if no mucosal abnormality was found on ileoscopy. However, in patient's management, histopathology examination was irreplaceable to establish patient's definite diagnosis.

Abnormal ileoscopy was found in 48 (80%) patients. This was different with other references where the macroscopic abnormalities were found only in 3.7–34% patients.<sup>10,12,13,15</sup> Similar to the studies performed in South Korea where from 3,417 subjects in the study, ileoscopy abnormalities were found in 125 (3.7%) subjects. However, this study was different

because subjects of the study were recruited from all patients who undergo ileoscopy, not only in patients with chronic diarrhea.<sup>12</sup> On the other hand, in the study conducted by McHugg et al, was ileoscopy abnormality found in 19.3% of the study subjects.<sup>9</sup>

This difference showed that ileoscopy examination still need to be performed although there is normal colonoscopy appearance. From 48 patients, 1 of them revealed normal histology appearance. This was found in polyp hyperplastic case. Most common abnormalities include chronic ileitis and ileitis which is in line with the appearance of inflammatory intestinal disease. This was similar to the study by Morini et al, in which 9 of 47 (6.5%) subjects exhibited ileitis appearance which were in concordance with Crohn's disease, and 38 (93.5%) subjects had chronic ileitis appearance.<sup>13</sup>

In this study, there was similar results between ileoscopy and histopathology examinations in 93.33% patients. This was slightly lower compared to the study conducted by Melo et al, in which the conformity between ileoscopy and histopathology examination reached up to 99.1%.<sup>5</sup> This difference was probably caused by difference in categorizing histopathology abnormalities. Melo et al in their study classified histopathology abnormality into 3 degrees, which were normal, mild ileitis, and moderate ileitis. Further, they combined the normal histopathology appearance and mild ileitis into one group, which was normal group before comparing with the ileoscopy examination. Meanwhile, this study did not categorize ileitis into those categories. Therefore, the number of abnormalities found were more.<sup>5</sup>

Chronic diarrhea is a disturbing problem in the community, and is one of the quite common referral cases in gastroenterology. In Western countries, the prevalence may reached up to 4–5% in the general population.<sup>2</sup> Although difficult to estimate, this problem will certainly cause disturbance in various field in the community, such as: in country economy field, loss of work productivity, and loss in paying disability. Current guideline recommended various types of examinations to help in establishing the diagnosis in chronic diarrhea cases, one of those is colonoscopy. Ileoscopy is a standard part in colonoscopy examination, and in several previous studies, this procedure revealed the increased of accuracy of colonoscopy diagnosis.<sup>10–13</sup>

In this study, from 60 patients with chronic diarrhea and normal colonoscopy, there was abnormality in ileoscopy results in 48 (80%) patients, and histopathology abnormality in 50 (83.33%) patients. This examination may assist in establishing diagnosis

in only 34 (56.7%) patients. This was different with other studies, such as in the study conducted by Morini et al, which reported that in non-bleeding chronic diarrhea cases, ileoscopy examination revealed ileum abnormalities in 34% cases, in which histopathology examination help in establishing the diagnosis of Crohn's disease in 5.8% cases.<sup>13</sup>

Other studies performed by Yusoff et al, in which in patients with normal colonoscopy, there was 13% ileoscopy abnormality, with 8% of them had non-specific histopathology abnormalities, and only in 5% patients, there was significant histopathology abnormalities to establish the diagnosis.<sup>15</sup> Other studies showed different results, which were 18% and the highest were 67% in patients with diarrhea and HIV.<sup>16</sup>

This difference may be caused by difference in establishing operational definition in determining abnormalities in ileoscopy results. Furthermore, difference in the sample size also influenced the results.

In this study, it was revealed that ileoscopy examination may help in establishing the diagnosis in 35 (58.3%) patients. Meanwhile, ileum histopathology examination might assist in establishing the diagnosis in 36 (60%) patients. This showed that histopathology examination had more contribution in establishing the diagnosis in patients.

## CONCLUSION

Based on this study, it could be concluded that ileoscopy examination in patients with chronic diarrhea and normal colonoscopy revealed similar results to the histopathology examination. This study may be further evaluated by making diagnostic study to compare other variables, such as: signs, symptoms, laboratory, and ileoscopy in diagnosing ileum abnormality in chronic diarrhea with normal colonoscopy.

## REFERENCES

1. Tabrizchie H, Zahedie MJ, Abasie MH, Jafari E, Haghdoost A, Hosseini SH. Frequency and distribution of microscopic findings in patients with chronic non-bloody diarrhea and normal colonoscopy. *Iran J Med Sci* 2008;33:101-5.
2. Thomas P, Forbes A, Green J, Howdle P, Long R, Playford R, et al. Guidelines for the investigation of chronic diarrhea, 2nd edition. *Gut* 2003;52:1-15.
3. Silva J, Brito TD, Damiao AOMC, Laudanna AA, Sipahi AM. Histologic study of colonic mucosa in patients with chronic diarrhea and normal colonoscopic findings. *J Clin Gastroenterol* 2006;40:44-8.
4. Simadibrata M, Rani A, Daldiyono, Syam AF, Tytgat GNJ, Yuwono V, et al. Diseases in chronic non-infective diarrhea. *Indones J Gastroenterol Hepatol Dig Endosc* 2004;5:15-8.

5. Melo M, Cury PM, Ronchi LS, Goncalves-Filho FA, Cunrath GS, Netinho JG. Terminal ileum of patients who underwent colonoscopy: endoscopic, histologic, and clinical aspects. *Arq Gastroenterol* 2009;46:102-6.
6. Sayilir A. Diagnostic value of terminal ileum biopsy in chronic diarrhea with normal endoscopic appearance. *J Digest Dis* 2011;1751-2980.
7. Shah R, Fenoglio-Preiser C, Bleau B, Giannella R. Usefulness of colonoscopy with biopsy in evaluation of patients with chronic diarrhea. *Am J Gastroenterol* 2001;96:1091-5.
8. Barta Z, Mekkel G, Csipo I, Toth L, Szakall S, Szabo GG, et al. Microscopic colitis: a retrospective study of clinical presentation in 53 patients. *World J Gastroenterol* 2005;11:1351-5.
9. McHugg J, Appelman HD, McKenna BJ. The diagnostic value of endoscopic terminal ileum biopsies. *Am J Gastroenterol* 2007;102:1084-9.
10. Cherian S, Singh P. Is routine ileoscopy useful? An observational study of procedure times, diagnostic yield, and learning curve. *Am J Gastroenterol* 2004;99:2324-9.
11. Misra S, Dwivedi M, Misra V, Gupta M, Kunwar BK. Endoscopic biopsies from normal-appearing terminal ileum and cecum in patients with suspected colonic tuberculosis. *Endoscopy* 2004;36:612-6.
12. Jeong S, Lee KJ, Kim YB, Kwon HC, Sin SJ, Chung JY. Diagnostic value of terminal ileum intubation during Colonoscopy. *J Gastroenterol Hepatol* 2008;23:51-5.
13. Morini S, Lorenzetti R, Stella F, Martini MT, Hassan C, Zullo A. Retrograde ileoscopy in chronic nonbloody diarrhea: a prospective, case-control study. *Am J Gastroenterol* 2003;98:1512-5.
14. Marshall J, Hewak J, Farrow R, Wright C, Riddell RH, Somers S, et al. Terminal ileal imaging with ileoscopy versus small-bowel meal with pneumocolon. *J Clin Gastroenterol* 1998;27:217-22.
15. Yusoff I, Ormonde DG, Hoffman NE. Routine colonic mucosal biopsy and ileoscopy increases diagnostic yield in patients undergoing colonoscopy for diarrhea. *J Gastroenterol Hepatol* 2002;17:276-80.
16. Zwas F, Bonheim NA, Berken CA, Gray S. Diagnostic yield of routine ileoscopy *Am J Gastroenterol* 1995;90:1441-3.

---

*Correspondence:*  
Ari Fahrial Syam  
Division of Gastroenterology  
Department of Internal Medicine  
Dr. Cipto Mangunkusumo General National Hospital  
Jl. Diponegoro No. 71 Jakarta Indonesia  
Phone: +62-21-3153957 Facsimile: +62-21-3142454  
E-mail: ari\_syam@hotmail.com

---