Available online at www.medicinescience.org

ORIGINAL RESEARCH

Medicine Science International Medical Journal

Medicine Science 2018;7(4):841-4

Prevalence of microscopic colitis in patients with chronic diarrhea

Gokhan Pektas[1], Meral Soylu Sozen[2], Ayhan Vurmaz[3], Osman Ersoy[4]

[1]Mugla State Hospital, Hematology Clinic, Mugla, Turkey
[2]Ataturk Training and Research Hospital, Internal Medicine Clinic, Ankara, Turkey
[3]Afyon Kocatepe University Faculty of Medicine Medical Biochemistry Clinic, Afyonkarahisar, Turkey
[4]Ataturk Training and Research Hospital, Gastroenterology Clinic, Ankara, Turkey

Received 26 March 2018; Accepted 21 May 2018
Available online 11.07.2018 with doi:10.5455/medscience.2018.07.8842

Abstract
Microscopic colitis affects nearly 10% of the patients with chronic diarrhea which is defined as an increase in the number of daily defecation or the amount of stool lasting more than 4 weeks. The present study aims to analyze the Prevalence of Microscopic Colitis in patients who have admitted to a tertiary health center due to chronic diarrhea with unidentified etiology. This is a retrospective review of 54 patients (31 men and 23 women) with chronic diarrhea who were admitted to the gastroenterology department of the study center between July 2009 and July 2010. Data related with the patient age, patient gender, laboratory findings and histopathological alterations were obtained from hospital files. The men and women included in this study were statistically similar with respect to their mean age (36.4 ±11.1 years vs 43.1 ±18.0 years, p=0.125). The male and female patients with cheronic diarrhea had statistically similar incidences of duodenitis (8/31 vs 11/23, 25.8% vs 47.8%, p=0.097). These men and women had also statistically similar incidences of terminal ileitis (10/31 vs 8/23, 32.3% vs 34.8%, p=0.847) respectively. The male and female patients with chronic diarrhea had statistically similar incidences of non-specific colitis (19/31 vs 12/23, 61.3% vs 52.2%, p=0.499). However, non-specific colitis was significantly more frequent in patients with normal duodenum biopsy than patients with duodenitis (24/35, 68.6% vs 7/19, 36.8%; p=0.008). Microscopic colitis should be considered in differential diagnosis of middle aged and elderly women with chronic diarrhea. Although there is no general consensus about the localization and number of intestinal biopsies, a large number of biopsies should be collected, even from the colon mucosa with normal macroscopic appearance in these patients.

Keywords: Chronic diarrhea, microscopic colitis, gastroenteritis

Introduction

Chronic diarrhea is defined as an increase in the number of daily defecation or the amount of stool which lasts more than 4 weeks. Microscopic colitis affects nearly 10% of the patients with chronic diarrhea and its incidence varies between 3.7% and 13% [1]. It was first described by Read et al. in 1980 as a moderate increase in the number of inflammatory cells in biopsies taken from normal-looking mucosa during sigmoidoscopy in the mucosa of the rectum and colon with chronic watery diarrhea [2]. This clinical entity usually represents as chronic, bloodless, waterry diarrhea in the fifth and sixth decades of life. The presence of nocturnal diarrhea helps to distinguish microscopic colitis from irritable bowel diseases [3,4].

Microscopic colitis has two subtypes which are namely lymphocytic colitis and collagenous colitis. Lymphocytic colitis refers to intraepithelial lymphocytosis while collagenous colitis is characterized by an increase in the subepithelial collagen thickness. Colonoscopy may demonstrate normal appearing or hyperemic mucosa in microscopic colitis. The incidences of collagenous colitis and lymphocytic colitis were reported as 0.6-5.2/100000 and 3.7-4.5/100000 in Northern America and Europe (5,6). As for Turkey, the incidence of lymphocytic colitis is 9% and the incidence of collagenous colitis is 2.5% in patients with chronic diarrhea [7].

The etiology of microscopic colitis is still unclear, abnormal immunoreaction to antigens, malabsorption of bile acids, HLA association and drugs (i.e., non-steroid anti-inflammatory agents, proton pump inhibitors, serotonine uptake inhibitors, beta blockers, statins, and bisphosphonates) have been proposed as the underlying factors. Clinical findings suggesting an underlying abnormal immune response include the presence of female dominance, the co-existence of autoantibodies and the association with autoimmune diseases such as celiac disease, thyroid diseases and spondyloarthritis [8,9].

The present study aims to analyze the patients who have admitted to a tertiary health center due to chronic diarrhea with unidentified etiology.

***Coresponding Author:** Ayhan Vurmaz, Afyon Kocatepe University Faculty of Medicine Medical Biochemistry Department, Afyonkarahisar, Turkey
E-mail: ayhan.vurmaz@gmail.com

Materials and Methods

The present study was approved by the Ethical Committe of Atatürk Research and Training Hospital. This is a retrospective review of 54 patients (31 men and 23 women) with chronic diarrhea who were admitted to the gastroenterology department of the study center between July 2009 and July 2010.

The patients who had chronic diarrhea (ongoing for more than four weeks) with unexplained etiology were included in this study. Those with a previous history of radiotherapy and chemotherapy, surgery regarding the gallbladder, stomach or colon, those who were diagnosed with irritable bowel syndrome, those with a known history of liver and kidney failure and those using laxatives and antibiotics were excluded.

Data related with the patient age, patient gender, laboratory findings and histopathological alterations were obtained from hospital files. The workup of the patients with chronic diarrhea consisted of normal stool microscopy and culture as well as laboratory tests within the normal spectrum. Hematological tests included complete blood count and erythrocyte sedimentation rate whereas biochemical evaluation referred to the measurement of glucose, urea, creatinine, hepatic transaminases, total protein, albumin, amylase, gastrin, total cholesterol, triglyceride, lipoprotein and thyroid stimulating hormone levels. Serological tests comprised C-reactive protein, anti-HIV, anti-gliadin and anti-endomysial antibody levels.

All patients underwent abdominal ultrasonography, upper gastrointestinal endoscopy and colonoscopy. There was nothing particular in the abdominal ultrasonography scans of the reviewed patients. The duodenum, jejunum and ileum were visualized by endoscopy while rectum, sigmoid colon and descending colon were assessed by colonoscopy. As the aforementioned anatomical regions all appeared normal macroscopically in each participant, several biopsies were obtained during endoscopy and colonoscopy. Acquired biopsies were examined by a single experienced pathologist working at the study center.

Results

The demographic and clinical characteristics of the reviewed patients are enlisted in Table 1. Duodenum biopsies of 35 patients were normal (64.8%) whereas 19 patients had duodenitis (35.2%). Ileum biopsies of 36 patients revealed nothing particular (66.7%) while 18 patients had terminal ileitis (33.3%). Colon biopsies of 20 patients were normal (37%), whereas 31 patients had non-specific colitis (57.3%). In addition, one patient had collagenous colitis (1.9%) and one patient had amebiasis (1.9%). One patient was diagnosed with malabsorption syndrome (1.9%) histologically due to the presence of villous blunting, lymphocytosis within intestinal epithelium and lymphocytic infiltrates along with apoptotic debris in the deeper mucosa.

The men and women included in this study were statistically similar with respect to their age (36.4 ±11.1 years vs 43.1 ±18.0 years, p=0.125). The male and female patients with chronic diarrhea had statistically similar incidences of duodenitis (8/31 vs 11/23, 25.8% vs 47.8%, p=0.097). Normal duodenum biopsy was detected at statistically similar rates in men and women reviewed by this study (23/31 vs 12/23, 74.2% vs 52.2%, p=0.097). The men and women in this study were statistically similar with respect to normal small bowel biopsy (21/31 vs 15/23, 67.7% vs 65.2%, p=0.847). The male and female patients with chronic diarrhea had statistically similar incidences of terminal ileitis (10/31 vs 8/23, 32.3% vs 34.8%, p=0.847).

Normal colon biopsy was detected at statistically similar rates in men and women reviewed by this study (11/31 vs 9/23, 35.5% vs 39.2%, p=0.499). The men and women with chronic diarrhea had also statistically similar incidences of non-specific colitis (19/31 vs 12/23, 61.3% vs 52.2%, p=0.499). However, non-specific colitis was significantly more frequent in patients with normal duodenum biopsy than patients with duodenitis (24/35, 68.6% vs 7/19, 36.8%; p=0.008).

Table 1. Demographic and Clinical Characteristics of the Participants

	Mean±Standard Deviation	Range (Minimum-Maximum)
Age (years)	39.3±14.7	20-87
Hemoglobin (g/dl)	14.2±1.9	8.1–18.3
Leukocyte count (k/µL)	7509.6±1894.7	4100.0–11400.0
Thrombocyte count (k/µL)	260890.5±57020.2	159000.0–432000.0
Erythrocyte sedimentation rate (mm/hour)	14.1±12.3	2.0–50.0
C-reactive protein (mg/L)	5.5±6.8	3.0–48.0
Fasting glucose (mg/dL)	93.5±9.6	72.0–112.0
Urea (mg/dL)	27.8±11.6	14.0–96.0
Creatinine (mg/dL)	1.0±0.2	0.6–1.6
Alanine transaminase (U/L)	30.0±28.2	5.0–169.0
Aspartate transaminase (U/L)	23.1±9.6	8.0–60.0
Total protein (g/dL)	7.3±0.7	4.1–8.2
Albumin (g/dL)	4.5±0.8	3.3–8.6
Total cholesterol (mg/dL)	163.8±40.5	95.0–285.0
Triglyceride (mg/dL)	127.0±75.2	36.0–445.0
Low density lipoprotein (mg/dL)	97.5±28.8	30.0–157.0
Gastrin (pg/ml)	65.0±24.6	33.0–183.0
Thyroid stimulating hormone (µIU/mL)	1.6±1.1	0.4–6.0

Discussion

Chronic diarrhea is the most common complaint of the patients who are examined at the gastroenterology departments. The frequency of chronic diarrhea is about 4% to 5% in Western populations and chronic diarrhea affects 7% to 14% of the elderly individuals. Microscopic colitis is observed in 4% to 13% of the patients who have waterry diarrhea with unknown etiology [10-13].

Epidemiological data obtained from the studies performed on microscopic colitis in different parts of the world are summarized in Table 2. According to these data, the majority of the microscopic colitis cases are reported from Northern America and Europe. The number of microscopic colitis patients analyzed in British and French studies is lower than the number of patients investigated by studies held in Northern America and other European countries [13-22].

The incidence of microscopic colitis might change over a period of time within the same country. A study published in 1993 detected microscopic colitis in 4% of the Swedish patients with chronic watery diarrhea, but the same value increased to 10% in 1998 [23, 24]. About 9.5% of the cases which underwent colonoscopy due to chronic diarrhea throughout a five-year period were diagnosed with lymphocytic colitis in a Spanish study [25]. A study by Marshall et al. identified lymphocytic colitis in 11.7% and collagenous colitis in 0.9% of 111 patients who had chronic diarrhea with unknown etiology [26]. Another study investigating 132 patients with chronic diarrhea and abdominal pain found lymphocytic colitis in 16% of the patients and collagenous colitis in 5% of the patients [27].

Collagenous colitis was detected in 0.8 of every 100000 Swedish citizens between 1984 and 1988, and this ratio increased to 4.9 between 1993 and 1998 and to 6.1 between 1996 and 1998 [23, 24]. Based on the health records kept between 1995 and 1999 in Iceland, the annual incidence values for collagenous colitis and lymphocytic colitis were calculated as 5.2/100000 and 4.0/100000, respectively [6].

As for Turkey, microscopic colitis was detected in 11.5% of the patients who had chronic diarrhea with unknown etiology [7]. Since only one patient was diagnosed with collagenous colitis, the frequency of microscopic colitis was found to be 1.9% in patients who have chronic diarrhea with unidentified etiology. Such a low frequency can be attributed to the relatively small cohort size and probable unawareness of the dealing pathologists about microscopic colitis.

The frequency of lymphocytic colitis is 4 to 20 times more than the frequency of collagenous colitis in European countries [13-18]. For instance, the frequency of lymphocytic colitis is three times more than the frequency of collagenous colitis in a Spanish study [25]. On the other hand, the frequency of lymphocytic colitis was four times more than the frequency of collagenous colitis in a Turkish study [7].

Microscopic colitis affects females more than males and more specifically, collagenous colitis affects women seven times more than men [1-9]. Swedish women have twice the risk of microscopic colitis than Swedish men [23,24] and the women in Iceland have five times more risk of being affected by microscopic colitis than men [6]. Similarly, Canadian women are 3.5 times more likely to have collagenous colitis and 7 times more likely to have lymphocytic colitis than Canadian men [28]. In addition, Spanish women are 4.7 times more likely to develop collagenous colitis and 2.7 times more likely to develop lymphocytic colitis than Spanish men [25]. However, Turkish men and women were found to be almost equally affected by microscopic colitis (1/1.4) [7]. A similar result was found in a Mexican study and it was reported that the ratio of men to women affected by microscopic colitis was 1/1.8 [29].

Epidemiological studies point out 68 years as the mean age of the patients with microscopic colitis (1-16). The mean age of the patients diagnosed with microscopic colitis was 56.5 years in a Mexican study [29] and 38.6 years in an Indian study [5]. However, microscopic colitis was diagnosed at a mean age of 45.0 years in a Turkish study [7]. The risk of being diagnosed with microscopic colitis was 5 times higher in Canadian patients aged ≥65 years [26].

The age of the lymphocytic colitis cases varied between 51 and 59 years while the age of the collagenous colitis cases varied between 64 and 68 years [13-16]. A Turkish study reported the mean age of lymphocytic colitis cases as 45 years (range 27-63 years) and the mean age of collagenous colitis cases as 60 years (range: 54-65 years) [7]. The only patient diagnosed with collagenous colitis was a 37-year-old woman in this study.

In conclusion, microscopic colitis should be considered in differential diagnosis of middle-aged and elderly women with chronic diarrhea. Since microscopic colitis significantly impairs the quality of life in patients, it is important to make an early diagnosis of this disease. Therefore, the physicians examining patients with chronic diarrhea, the gastroenterologists performing the endoscopy, and the pathologists evaluating gastrointestinal biopsies should have knowledge and insight about microscopic colitis. Colonoscopy should be performed in all patients who have chronic waterry diarrhea with unidentified etiology and the gastroenterologists performing colonoscopy should take biopsies from the intestinal mucosa despite its normal macroscopic appearance. Although there is no general consensus about the localization and number of intestinal biopsies, a large number of biopsies should be collected, even from the colon mucosa which appeared macroscopically normal. Further research is warranted to clarify the role of microscopic colitis in Turkish patients who have chronic non-bloody diarrhea with unknown etiology.

Table 2. Epidemiological Data on Microscopic Colitis

	Collagenous colitis	Lymphocytic colitis
Orebro, Sweden /1984–1988 (31)	0.8	
Orebro, Sweden /1989–1993 (31)	2.7	
Orebro, Sweden /1993–1995 (32)	3.7	3.1
Orebro, Sweden /1996–1998 (32)	6.1	5.7
Franche-Comté, Fransa/1987–1992 (33)	0.6	
Terrassa, Spain /1993–1997 (34)	2.3	3.7
Iceland /1995–1999 (35)	5.2	4.0
Olmsted County, †USA/1985–1989 (36)	0.3	0.5
Olmsted County, USA/1990–1993 (36)	1.6	1.0
Olmsted County, USA/1994–1997 (36)	3.9	6.4
Olmsted County, USA/1997–2001 (36)	6.2	12.9
Lothian, İngiltere/1998–2003 (37)	0.8	
Tayside, United Kingdom /1999–2004 (23)	1.1	0.6

USA: United States of America
Incidence values are reported as per 100000 patients.

Competing interests
The authors declare that they have no competing interest

Financial Disclosure
The financial support for this study was provided by the investigators themselves.

Ethical approval
The present study was approved by the Ethical Committe of Atatürk Research and Training Hospital.

References

1. Datta I, Brar SS, Andrews CN, et al. Microscopic colitis: a review for the surgical endoscopist. Can J Surg. 2009;52:E167-72.
2. Read NW, Krejs GJ, Read MG, et al. Chronic diarrhea of unknown origin. Gastroenterol. 1980;78:264-71.
3. Okamoto R, Negi M, Tomii S, et al. Diagnosis and treatment of microscopic colitis. Clin J Gastroenterol. 2016;9:169-74.
4. Stoicescu A, Becheanu G, Dumbrava M, et al. Microscopic colitis-a missed diagnosis in diarrhea-predominant irritable bowel syndrome. J Clin Med. 2012;71:3-9.
5. Misra V, Misra SP, Dwivedi M, et al. Microscopic colitis in patients presenting with chronic diarrhea. Indian J Pathol Microbiol. 2010;53:15-9.
6. Gentile NM, Khanna S, Loftus EV, et al. The epidemiology of microscopic colitis in Olmsted County from 2002 to 2010: a population-based study. Clin Gastroenterol Hepatol. 2014;12:838-42.
7. Erdem L, Yıldırım S, Akbayır N, et al. Prevalence of microscopic colitis in patients with diarrhea of unknown etiology in Turkey. World J Gastroenterol. 2008;14:4319-23.
8. Ianiro G1, Cammarota G, Valerio L, et al. Microscopic colitis. World J Gastroenterol. 2012;18:6206-15.
9. Storr MA. Microscopic colitis: epidemiology, pathophysiology, diagnosis and current management-an update 2013. ISRN Gastroenterol. 2013;2013: 352718.
10. Thomas PD1, Forbes A, Green J, Guidelines for the investigation of chronic diarrhoea, Gut. 2003;52:1-15.
11. Nhylin N, Bohr J, Eriksson S, et al. Systematic review: microscopic colitis. Aliment Pharmacol Ther. 2006;23:1525-34.
12. Netzer P, Levkovits H, Zimmermann A, et al. Collagen colitis and lymphocytic (microscopic) colitis: different or common origin? Z Gastroenterol. 1997;35:681-90.
13. Raclot G, Queneau PE, Ottignon Y. Incidence of collagenous colitis. A retrospective study in the east of France. Gastroenterol. 1994;106:A23.
14. Rajan J, Noble C, Anderson C, et al. The epidemiology and clinical features of collagenous colitis in Lothian. Gut. 2005;54:A99.
15. Heron T, Walsh S, Mowat A. Microscopic colitis in tayside: clinical features, associations, and behaviour. Gut. 2005;54: A84.
16. Burch VC, Price SK, Wright JP, et al. Collagenous colitis-a rare cause of chronic watery diarrhoea. A case report. S Afr Med J. 1992;81:617-9.
17. Narita T, Akiyama M. Collagenous colitis in a Japanese patient. Pathol Int. 1996;46:211-5.
18. Valle Mansilla JL, Leon Barua R, Recavarren Arce S, et al. Microscopic colitis in patients with chronic diarrhea. Rev Gastroenterol Peru. 2002;22:275-8.
19. Tagkalidis PP, Gibson PR, Bhathal PS. Microscopic colitis demonstrates a T helper cell type 1 mucosal cytokine profile. J Clin Pathol. 2007;60:382-7.
20. Pokorny CS, Kneale KL, Henderson CJ. Progression of collagenous colitis to ulcerative colitis. J Clin Gastroenterol. 2001;32: 435-8.
21. Pokorny CS, Selby WS. Microscopic colitis: An underdiagnosed cause of chronic diarrhoea-the clue is in the biopsies. Intern Med J. 2003;33:305-9.
22. Saurine TJ, Brewer JM, Eckstein RP. Microscopic colitis with granulomatous inflammation. Histopathol. 2004;45:82-6.
23. Olesen M, Eriksson S, Bohr J, Microscopic colitis: a common diarrhoeal disease. An epidemiological study in Orebro, Sweden, 1993-1998. Gut. 2004;53:346-50.
24. Olesen M, Eriksson S, Bohr J, Lymphocytic colitis: a retrospective clinical study of 199 Swedish patients. Gut. 2004;53:536-41.
25. Fernandez-Banares F, Salas A, Forne M, et al. Incidence of collagenous and lymphocytic colitis: A 5-year population-based study. Am J Gastroenterol. 1999;94:418-23.
26. Marshall JB, Singh R, Diaz-Ariaz AA. Chronic, unexplained diarrhea: are biopsies necessaryif colonoscopyis normal. Am J Gastroenterol. 1995;372-6.
27. Gineston JL, Sevestre H, Descombes P, et al. Biopsies of the endoscopically normal rectum and colon: a necessity; incidence of collagen colitis and microscopic colitis. Gastroenterol Clin Biol. 1989;13:360-3.
28. Williams JJ, Kaplan GG, Makhija S, et al. Microscopic colitis-defining incidence rates and risk factors: A population-based study. Clin Gastroenterol Hepatol. 2008;6:35-40.
29. Rubio-Tapia A, Martínez-Salgado J, García-Leiva J, et al. Microscopic colitides: a single center experience in Mexico. Int J Colorectal Dis. 2007;22:1031-6.
30. Falodia S, Makharia GK, Sateesh J, et al. Spectrum of microscopic colitis in a tertiary care centre in India. Trop Gastroenterol. 2007;28:121-5.
31. Veress B, Löfberg R, Bergman L. Microscopic colitis syndrome. Gut. 1995;36:880-9.
32. Riddell RH, Tanaka M, Mazzoleni G. Non-steroidal antiinflammatory drugs as a possible cause of collagenous colitis: a case-control study. Gut. 1992;33:683-6.
33. Genova G1, Arena N, Guddo F, Collagenous colitis: Morphologic and immunohistochemical study. Pathologica. 1993;85:489-95.
34. Golf JS, Barnett JL, Pelke T, et al. Collagenous colitis: histopathology and clinical course. Am J Gastroenterol. 1997;92:57-60.
35. Baert F, Wouters K, D'Haens G. Lymphocytic colitis: a distinct clinical entity? a clinicopathological confrontation of lymphocytic and collagenous colitis. Gut. 1999;45:375-9.
36. Wilcox GM, Mattia AR. Microscopic colitis associated with omeprazole and esomeprazole exposure. J Clin Gastroenterol. 2009;45:451-3.
37. Fernández-Bañares F, Esteve M, Espinós JC, et al. Drug consumption and the risk of microscopic colitis. Am J Gastroenterol. 2007;102: 324-30.