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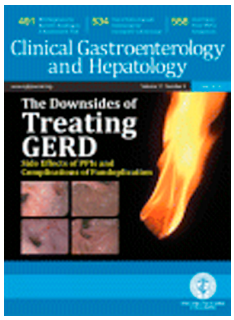

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INTRODUCTION

Microscopic colitis (MC) is a chronic inflammatory disease of the colon that presents with chronic, non-bloody watery diarrhea and only few or no endoscopic abnormalities. Histologic examination discriminates lymphocytic colitis (LyC; presence of ≥20 intraepithelial lymphocytes per 100 surface epithelial cells) and collagenous colitis (CC; colonic subepithelial collagen band >10 micrometers in diameter).[1,2] MC not otherwise specified (NOS) describes a subgroup of patients who do not fulfill the diagnostic criteria for either CC or LyC.[1,2] Population-based epidemiologic data regarding MC are scarce. We aimed to evaluate the clinical presentation at diagnosis, incidence and prevalence of MC in Cantons of Vaud and Fribourg, Switzerland.

METHODS

Cantons of Vaud and Fribourg lie in the French speaking, Western part of Switzerland. As of 12/2017, both cantons together had a population of 1,109,230 inhabitants. After having identified MC patients through databases of all Pathology institutes (n=6) serving both cantons and a histology slide review to assure correctness of diagnosis, we performed a chart review in practices of all gastroenterologists covering both cantons (n=42). The study was approved by the ethics committee of Cantons of Vaud and Fribourg (CER-VD 306/15). Two hundred and fifty-two patients with MC, diagnosed between January 1994 and December 2017, were identified. Of these, 34 were excluded for having NOS. We

calculated incidence rates using data provided by the Institutes of population statistics of Canton of Vaud and Fribourg.

RESULTS

Of the 218 patients with MC, 123 (56.4%) had LyC and 95 (43.6%) had CC. Seventy-four percent (162/218) of MC patients were female, mean age at first symptoms was 62±15.4 years (range 24-89), mean age at MC diagnosis was 63.2±14.3 years (range 29-89). All MC patients suffered from diarrhea, followed by abdominal pain (31.7%), weight loss (31.2%), bloating (20.6%), fatigue (9.6%), nausea / vomiting (3.2%). Exposure to risk factors for MC were frequently found and included HMG-CoA reductase inhibitors (27.1%), non-steroidal anti-inflammatory drugs (14.2%), proton-pump inhibitors (22.5%), serotonine reuptake inhibitors (22.5%), and smoking (20.2%). Infectious agents were searched and excluded as cause of chronic diarrhea in all included patients.

A colonoscopy was performed as diagnostic tool in all of the 218 patients. In 74.3% of patients the colonoscopy was normal. Polyps were found in 16.5% of MC patients, followed by edema (9.2%), erythema (4.6%), and an erosion (0.5%). Median thickness of the subepithelial collagen band in patients with CC was 25µm, whereas patients with LyC had a median of 35 intra-epithelial lymphocytes per 100 epithelial cells.

Oral budesonide was most frequently used as first therapy (72.9%), followed by loperamide (66.1%), aminosalicylates (16.1%), and cholestyramine (12.8%).

Incidence rates were calculated and are shown together with the cumulative prevalence in **Table 1**. No patient was diagnosed with MC prior to 1994. Incidence of MC significantly increased from 0.36/100,000 person-years in 1994-1997 to 6.85/100,000 person-years in 2017 (p=0.025, trend test). The cumulative prevalence of MC, LyC, and CC in 2017 was 19.65/100,000, 11.09/100,000, and 8.56/100,000, respectively. As such, the current prevalences for MC, LyC, and CC are 1/5,088 persons, 1/9018 persons, and 1/11,676 persons, respectively.

DISCUSSION

Our population-based study from Western Switzerland found a steady increase in incidence of MC during the last two decades. Findings of our study are in accordance with the results of a systematic review and meta-analysis that reported pooled incidence rates for CC of 4.14 (95% CI 2.89-5.40) per 100,000 person-years and 4.85 (95% CI 3.45-6.25) for LyC. Bergman et al. assessed the incidence of MC in Sweden from 1995-2015 in a nationwide cohort. Among 13,844 patients, incidence of MC was 10.5/100,000 as from 2006 which is roughly 6 times higher when compared to our findings.[4] Our data are comparable with the results of Fernandez-Banares et al. who found lower incidences (2.2/100,000 for LyC and 2.6/100,000 for CC) among 290,000 inhabitants in Spain.[5] These results reinforce the existence of a north-south gradient of MC which has been described by several groups.[3]

Strengths of our study are that all gastroenterologists and pathologists working in Cantons of Vaud and Fribourg collaborated in this project which is

crucial for the generation of population-based data. Limitations of our study are related to its retrospective design that impairs the generation of high-quality data to evaluate questions regarding the natural history of MC such as therapeutic response to different drugs.

In conclusion, in the first Swiss population-based study we found that MC incidence was steadily increasing over the last two decades. Compared to other countries, MC incidences are low in the population we studied.

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REFERENCES

1 Münch A, Dust A, Bohr J, Bonderup O, Fernandez-Banares F, Hjortswang H, et al. Microscopic colitis : current status, present and future challenges. J Crohns Colitis 2012;6:932-45.

2 Nguyen GC, Smalley WE, Vege SS, Carrasco-Labra A, and the Clinical Guidelines Committee: American gastroenterological association institute guideline on the medical treatment of microscopic colitis. Gastroenterology 2016;150:242-6.

3 Tong J, Zheng Q, Zhang C, Lo R, Shen J, Ran Z. Incidence, prevalence, and temporal trends of microscopic colitis: a systematic review and meta-analysis. Am J Gastroenterol 2015;110:265-76.

4 Bergman D, Clements MS, Khalili H, Agréus L, Hultcrantz R, Ludvigsson JF. A nationwide cohort study of the incidence of microscopic colitis in Sweden. Aliment Pharmacol Ther 2019;49:1395-1400.

5 Fernandez-Banares F, Salas A, Esteve M, Pardo L, Casalots J, Forne M, et al. Evolution of the incidence of collagenous colitis and lymphocytic colitis in Terrassa, Spain: a population-based study. Inflamm Bowel Dis 2011;17:1015–20.

TABLES

Table 1: Incidence (plus 95% confidence intervals) and prevalence of MC, LyC, and CC from 1994 to 2017. The incidence is shown per 100,000 inhabitants, stratified according to 4 year intervals and per year. The prevalence was calculated per 100,000 inhabitants at the end of the respective 4 year interval.

Interval	**1994-1997**	**1998-2001**	**2002-2005**	**2006-2009**	**2010-2013**	**2014-2017**
Population Vaud + Fribourg	839,965	856,091	901,168	967,802	1,027,985	1,109,230
MC new cases	3	8	22	45	64	76
MC incidence per 4 year interval	0.36, 0-0.48	0.93, 0.48-1.4	2.44, 2.2-2.68	4.7, 3.32-5.8	6.23, 5.44-7	6.85, 6.12-7.56
MC incidence per year	0.09	0.23	0.61	1.18	1.56	1.71
MC prevalence	0.36	1.29	3.66	8.06	13.81	19.65
LyC new cases	1	5	16	27	35	39
LyC incidence per 4 year interval	0.12, 0-0.48	0.58, 0.48-0.92	1.78, 1.32-2.2	2.79, 2.48-3.32	3.41, 2.72-3.88	3.52, 2.88-3.96
LyC incidence per year	0.03	1.5	0.45	0.7	0.85	0.88
LyC prevalence	0.12	0.7	2.44	5.06	8.17	11.09
CC new cases	2	3	6	18	29	37
CC incidence per 4 year interval	0.24, 0-0.48	0.35, 0-0.48	0.67, 0.48-0.89	1.86, 1.24-2.48	2.92, 2.72-3.12	3.34, 2.88-3.6
CC incidence per year	0.06	0.09	0.17	0.47	0.73	0.84
CC prevalence	0.24	0.58	1.22	2.99	5.64	8.56

TABLES

Table 1: Incidence (plus 95% confidence intervals) and prevalence of MC, , LyC and CC from 1994 to 2017. The incidence is shown per 100,000 inhabitants, stratified according to 4 year intervals and per year. The prevalence was calculated per 100,000 inhabitants at the end of the respective 4 year interval.

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