



## Original article

# Diarrhoea is not the only symptom that needs to be treated in patients with microscopic colitis<sup>☆</sup>



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## ABSTRACT

**Background:** Many patients with microscopic colitis (MC) also suffer from symptoms of irritable bowel syndrome (IBS), but the only treatment given is corticosteroids for the diarrhoea. The aim of this study was to examine how social factors, life style factors and drug treatment affect symptoms and well-being in patients suffering from MC.

**Methods:** Women, over the age of 73 years, with biopsy-verified MC, at any Departments of Gastroenterology, Skåne, between 2002 and 2010 were invited. The questionnaires Gastrointestinal Symptom Rating Scale (GSRS) and Psychological General Well-being Index (PGWB) were sent by mail, along with questions about social and life style factors, and medical history.

**Results:** Of 240 invited, 158 patients (66%) were included (median age 63 years, range 27–73 years). Only 26% had never smoked. Smoking and concomitant IBS were associated with both impaired gastrointestinal symptoms (OR = 3.96, 95% CI = 1.47–10.66 and OR = 4.40, 95% CI = 2.09–9.26, respectively) and impaired psychological well-being (OR = 2.77, 95% CI = 1.04–7.34 and OR = 3.82, 95% CI = 1.83–7.99, respectively). Treatment with proton pump inhibitors (PPI) was associated with increased gastrointestinal symptoms (OR = 3.44, 95% CI = 1.45–8.16). Age, social factors, and corticosteroids had no effect on symptoms or well-being. Smoking was the only risk factor associated with IBS (OR = 2.68, 95% CI = 1.115–6.26). **Conclusion:** Smoking and IBS are associated with impaired gastrointestinal symptoms and psychological well-being in MC patients. PPI is associated with impaired gastrointestinal symptoms.

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## 1. Introduction

Microscopic colitis (MC) is a an overall term for two conditions, collagenous colitis (CC) and lymphocytic colitis (LC), both characterized by chronic or recurrent watery diarrhoea, normal or near-normal endoscopic appearance, and specific microscopic abnormalities in colonic biopsies. However, these two disease entities can be considered together and stratified for subtypes [1]. Some studies have shown a female predominance in both CC and LC [2], mainly affecting middle-aged women, whereas others have not been able to confirm this in LC [3,4]. The aetiology to MC is unknown, but autoimmunity, inflammation and bile acid malabsorption have been suggested [2,5]. It is described that MC impairs health-related quality of life (HRQOL) [6]. Several studies have shown a symptomatic overlap between MC and irritable bowel syndrome (IBS) [7,8], and the combination of these two diseases further impairs gastrointestinal symptoms and psychological well-being [8].

The great overlap between IBS and MC, the fact that 63% of MC patients only have a single attack of diarrhoea, and the wide range of conditions rendering secondary MC, may lead to an inaccurate diagnose-setting [1,3,9]. Regarding inflammatory bowel disease (IBD), a consensus has been stated that requires at least one relapse of the disease before a final diagnosis [10]. This requirement is not at hand for MC, but has to be considered for the future. Irritable bowel syndrome is more common in women than in men, and as HRQOL and experiences of symptoms differ between genders, both IBS and MC should be studied separately for women and men [11].

Life style factors such as smoking, drinking and physical activity may be of importance, since these factors affect the gastrointestinal tract, psychological well-being, and HRQOL [12–14]. Smoking is a known risk factor for developing MC [15], but its effect on symptoms when the disease is present has never been examined. The wine consumption amongst women has been steadily increasing in Sweden during the last decades, coincident with the same time interval when MC has increased in incidence [2,16]. It is known that women are more vulnerable to alcohol than men [17]. The effect of physical activity on symptoms in MC has never been studied, although physical activity has a positive effect on IBS symptoms [13]. The patients are elder, thus often retired and living alone, which could further impair psychological well-being.

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Corticosteroid treatment is considered the gold standard as treatment of MC, and is the drug most frequently prescribed [2,5]. As more than half of the patients suffer from abdominal pain in addition to MC, treatment with sole corticosteroids should not be enough [8]. The goal for the treatment must be to improve all gastrointestinal symptoms and psychological well-being, why it is important to identify factors influencing these aspects. The aim of the present study was to examine the influence of social and life style factors such as marital status, education degree, employment, smoking habits, wine consumption, physical activity and drug treatment on gastrointestinal symptoms and psychological well-being in patients suffering from MC.

## 2. Methods

The study protocol was approved by the Ethics Committee of Lund University, and all participants gave written, informed consent when taking part in the study. The participation in the study was voluntary, with the possibility of withdrawal at any stage without any consequences, and that their responses would be treated confidentially.

### 2.1. Patients

Women who had been treated for MC at any outpatient clinic of the Departments of Gastroenterology, Skåne, between 2002 and 2010, were identified by search for the ICD-10 classification for the two forms collagenous colitis (CC) and lymphocytic colitis (LC). Only the 240 patients who had the diagnoses verified by colonic biopsy and were at the age of 73 years or younger, were invited to participate in the present study. About one-third of the total numbers of identified patients were excluded due to age above 73 years, as they had many other concomitant diseases and drug therapies. Altogether, 159 of the 240 invited patients accepted and were recruited to the study, but one patient was excluded due to another IBD diagnosis a few weeks after the inclusion. Leaving 158 patients (66%), and out of these, 133 (55%) also agreed to provide blood samples. These patients represent the majority of female cases of diagnosed MC in the most southern parts of Sweden under the age of 73 years.

### 2.2. Study design

Between March and June 2011, invitations including study information and questionnaires about marital status, education, employment, smoking habits, wine consumption, physical activity, medical history, gastrointestinal symptoms, psychological well-being and Rome III criteria were sent by mail to all 240 women. They were also invited to visit the outpatient clinics of the Departments of Gastroenterology, Skåne University Hospital, Malmö or Central Hospital in Kristianstad, to provide blood samples for routine analyses at the Departments of Laboratory Medicine in Skåne at respective hospital. Questionnaires were completed 1–3 weeks before blood samples were collected. A reminding letter was sent a month after the invitation letter to those who hadn't answered. Medical records were scrutinized and age, gastrointestinal symptoms, duration of symptoms, examinations, and treatments were recorded. Patients were divided into two groups. One group included patients with at least two episodes of watery diarrhoea; and/or dependent on long-term treatment of corticosteroids to maintain remission; and/or two pathological intestinal mucosa biopsies (MC1,  $n = 88$ ). The other group included patients who had concomitant coeliac disease (11 cases), had gone through an acute gastroenteritis briefly prior to the diagnostic colonoscopy (4 cases), only had had one episode of severe diarrhoea, or had had a normal biopsy after the initial pathological intestinal biopsy, along with clinical remission (MC2,  $n = 70$ ).

### 2.3. Questionnaires

#### 2.3.1. Gastrointestinal Symptom Rating Scale (GSRS)

The GSRS is a Swedish, disease-specific and self-administered questionnaire, designed to evaluate perceived severity of gastrointestinal symptoms during the previous week [18–20]. The questionnaire includes 15 items and uses a 7-grade Likert scale. This gives a total range value between 15 and 105 where the highest score (seven) represent the most pronounced symptoms and the lowest (one) no symptoms. The items are divided into five dimensions representing Reflux Syndrome (two items), Abdominal Pain Syndrome (three items), Constipation Syndrome (three items), Indigestion Syndrome (four items) and Diarrhoea Syndrome (three items). Norm values for healthy, gender-matched population is available. The control group consists of 2162 subjects (median age 51 (range 19–84) years), out of 4624 individuals from the city of Malmö, Sweden. Selection of the individuals was performed using a computerized allocation program. The strata consisted of women and men in six age groups [21].

#### 2.3.2. Psychological General Well-Being Index (PGWB)

The PGWB is a broad questionnaire to measure subjective well-being or distress during the previous week [22]. The questionnaire includes 22 items and uses a 6-grade Likert scale. This gives a total range value between 22 and 132 where a low score (one) correspond to a poor level of well-being and the higher value, the better psychological well-being. The items are divided into six dimensions representing Anxiety (five items), Depressed mood (three items), Positive well-being (four items), Self-control (three items), General health (three items) and Vitality (four items). Norm values for healthy, gender-matched population is available, see above [21].

#### 2.3.3. Rome III criteria

The patients completed a shortened version of the Rome III questionnaire, only including IBS symptoms [23]. This questionnaire has been translated and validated into the Swedish language (Magnus Simrén and Anna Rydén). Patients who fulfilled the criteria for Rome III were classified as also suffering from IBS, but as their diagnosis was MC, we have in accordance to its presence in IBD, called it IBS-like symptoms [8].

### 2.4. Statistical analyses

Statistical calculations were performed in SPSS, version 20.0 for Windows<sup>®</sup>. First, the distribution was tested using a one-sample Kolmogorov–Smirnov test. All distributions differed significantly ( $p < 0.05$ ) from a normal distribution, why studied factors were categorized. Values are given as median (interquartile range). We used simple mean imputation for missing data in GSRS and PGWB, when at least 50% of the items had been completed. There was no difference between CC and LC in the GSRS or PGWB scores or patient characteristics (data not shown), why all calculations were performed on the whole MC group, independent of CC or LC. The scores of the GSRS and PGWB were divided into dichotomy variables to get low or high values in the questionnaires. The dichotomy of best physical and psychological well-being was set as reference. Age was divided into 5-years intervals. The cohort was divided into quartiles of the number of days drinking wine, and the average number of minutes exercising per week during the year. Smoking was divided into three categories: subjects who had never smoked, subjects who had stopped smoking, and current smokers, including both regular and occasional smokers. Employment was divided into three categories: employed, retired, or others, where others included housewives, students or unemployed. There were missing values in wine consumption and education degree, which were labelled as an own category. The first category was used as reference. Factors intended to study (independent variables), namely, age, marital status, education degree, employment, smoking habits, days of wine consumption per month, physical activity

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