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Alimentary Tract

Incidence of microscopic colitis in the Netherlands. A nationwide population-based study from 2000 to 2012

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ABSTRACT

Background: Incidence rates of microscopic colitis are mainly based on regional data from a limited number of countries. To evaluate geographical differences and changes over time, more nationwide incidence rates are needed.
Aims: The aim of this retrospective study was to assess the incidence rate of microscopic colitis in the Netherlands in a nationwide cohort.
Methods: A search was performed in the Dutch pathology registry, covering records of all approximately 16.5 million inhabitants. Incident cases were defined as a first diagnosis of microscopic colitis (collagenous or lymphocytic colitis) between 2000 and 2012.
Results: In total, 7228 incident cases were identified with a mean annual incidence rate of 3.4 per 100,000 person years. Collagenous colitis was present in 3741 cases and lymphocytic colitis in 2718 cases, with a mean annual incidence rate of 1.8 and 1.3 per 100,000 person years, respectively. Remaining 769 cases were described as undefined microscopic colitis. Collagenous and lymphocytic colitis incidence rates increased significantly over time ($p < 0.001$) with a male:female ratio of 1:3 and 1:2, respectively.
Conclusion: The Dutch mean annual incidence rates of collagenous and lymphocytic colitis were considerably lower than previously reported by other countries. However, incidence rates increased gradually over time, with a clear female predominance.

1. Introduction

Microscopic colitis (MC) is an umbrella term for chronic watery diarrhoea with a normal endoscopic appearance of the colonic mucosa, and characteristic histological abnormalities. MC includes two subtypes, *i.e.* collagenous colitis (CC) and lymphocytic colitis (LC) [1,2]. Histologically, the hallmark of CC is the presence of a thickened subepithelial collagen layer (10 μm or more), whereas LC is characterized by an increased number of intraepithelial leukocytes [3–5]. Both MC entities are predominantly found in females over 65 years of age [6]. Whether CC and LC can be considered histopathological variants of the same disease or two different clinical entities is still matter of discussion [7–9]. Clinically, both CC and LC are characterized by a chronic relapsing course [10,11]. Although MC is successfully treated with oral budesonide in most cases, the relapse rate after cessation of treatment is 50–80% [12]. The chronic, relapsing, watery diarrhoea is the main contributor to the significantly decreased quality of life in MC patients [13–15].

Epidemiological studies performed in Sweden reported mean annual incidence rates up to 5.4 per 100,000 person years for CC in 2005–2010 [16] and 4.5 per 100,000 person years for LC in 2004–2008 [17]. Data collected in the US (Olmsted County, Minnesota) between 2002 and 2010, showed incidence rates of 7.1 and 9.5 per 100,000 person years for CC and LC, respectively [18], while a recent Spanish study [19] reported incidence rates of 2.6 and 2.2 per 100,000 person years between 2004 and 2008 for CC and LC, respectively. Most of the epidemiological studies described an increase in incidence rates over time

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[12,19–21], but recent follow-up data of two long-term, regional cohorts showed a stabilization of the incidence rates of both CC and LC over the last 10–15 years [17,18]. Although differences between countries seem to be present, the number of studies is too limited to draw firm conclusions on the geographical distribution of MC and changes over time.

The majority of epidemiological studies reporting MC incidence rates were based on regional data with populations up to 650,000 inhabitants [16–27]. Only one nationwide study was published so far, covering a rather small population of 277,184 inhabitants [28]. To evaluate potential geographical difference and changes over time, and to estimate the disease burden of MC in future, more data on long-term, nationwide incidence rates are warranted. Therefore, the aim of the present study was to assess the mean annual incidence rate of MC in the Netherlands in a nationwide, population-based cohort, spanning a thirteen-year period.

2. Materials and methods

2.1. Catchment area

Data on age, size, and sex distribution of the Dutch population between January 1, 2000 and December 31, 2012, were obtained *via* Statistics Netherlands (www.cbs.nl). In this time period the total population increased with 5.8%, from 15,863,950 inhabitants in 2000 to 16,778,025 in 2012. The age and sex distribution in 2000 and 2012 is shown in Fig. 1.

2.2. Pathology registry

The Netherlands has 55 pathology departments on a total of 132 hospitals, of which eight are university hospitals. Each pathology report generated in the Netherlands is archived in the nationwide registry of histo- and cytopathology, called PALGA [29]. This database was established in 1971 by the PALGA-foundation and reached full national coverage from 1991 onwards. Pathology reports are received on a daily basis and are automatically transposed into standardized excerpts containing encrypted patient data, a pathologist's conclusion, and a PALGA-diagnosis based upon the Dutch version of the Systemized Nomenclature of Medicine (SNOMED) [29].

2.3. Patient identification

For this retrospective study, a search was performed in the PALGA registry, using the following search terms: microscopic colitis, collagenous colitis, and lymphocytic colitis. The initial selection included any subject with at least one excerpt, generated between January 1, 2000 and December 31, 2012, in which the term MC, CC, or LC was mentioned. Subsequently, all registered colon biopsies of each subject meeting the search criteria were added in order to ascertain selection of incident cases only. The process of patient identification is schematically presented in Fig. 2. Excerpt evaluation was performed by a trained investigator (BV) after agreement on the diagnostic criteria with an experienced pathologist (AD). Patients' sex, age, and year of diagnosis were recorded. The year of diagnosis was defined as the year in which a positive diagnosis of CC, LC, or undefined MC (uMC) was reported for the first time. Incident cases were defined as a first diagnosis of CC, LC, or uMC between January 1, 2000 and December 31, 2012. Each incident case was included only once, regardless of a change in MC subtype or a suggested recurrence in later biopsies.

2.4. Diagnostic criteria

The generally accepted diagnostic criteria for CC and LC were applied [6]. Besides chronic inflammatory changes in the lamina propria and a damaged surface epithelium, this included a thickened subepithelial collagen layer (≥10 μm) for CC and an increased number of intraepithelial leukocytes (IEL ≥20/100 epithelial cells) without a thickened collagen layer for LC [2,5]. If no information for further subtyping was available, cases were classified as uMC. This term was chosen to avoid any confusion with the term 'incomplete microscopic colitis', which is used for patients with typical MC symptoms not fulfilling the strict histologic criteria for either CC or LC [25]. When features of both CC and LC were mentioned, cases were classified as the subtype most prominently present. However, PALGA excerpts consist of a pathologist's conclusion solely, frequently leaving specific diagnostic criteria unmentioned. Therefore, the likelihood of the diagnosis was determined for each evaluated excerpt, based on the pathologist's description. Together with an experienced pathologist (AD), the probability to comply with the diagnosis was defined as definite, probable, possible, or unlikely. Cases meeting the specific diagnostic criteria, or cases described as *e.g.* 'compatible with CC' or 'may very well fit LC' were

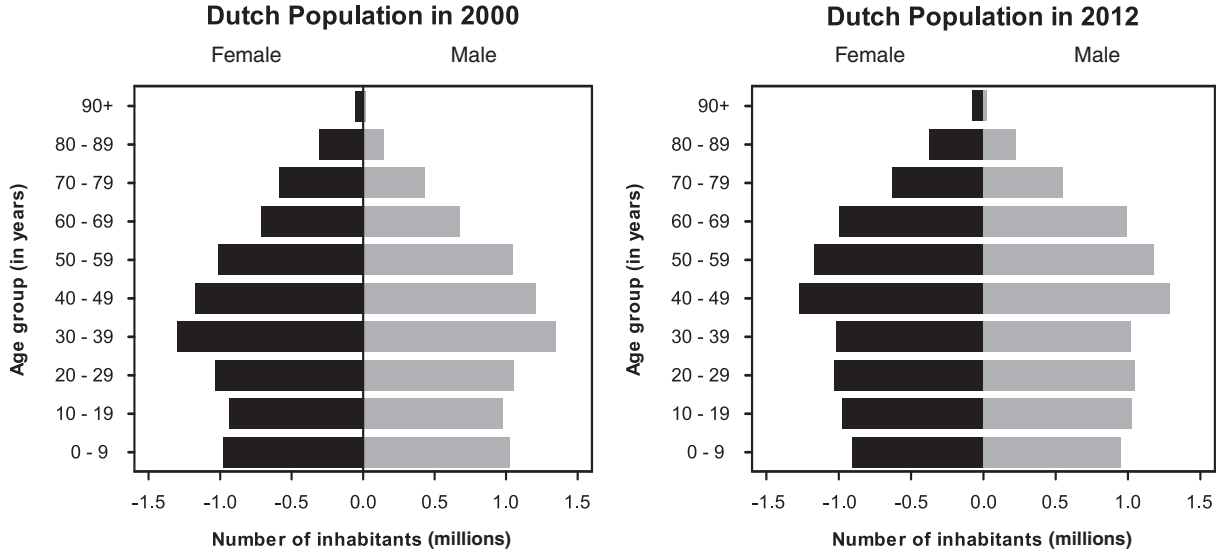

Fig. 1. Age pyramid of the Dutch population at December 31, 2000 (left) and December 31, 2012 (right).