

Seasonal variations in the onset of ulcerative colitis

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Abstract

Several retrospective studies have reported seasonal variations in the relapse of ulcerative colitis, and two studies have found seasonality in the onset of ulcerative colitis, with a peak from August to January. This study was designed to investigate possible seasonal variations of onset of ulcerative colitis (UC) and Crohn's disease (CD). Patients with symptoms of one year or less were recruited from a prospective study of the incidence of inflammatory bowel disease, and the onset of symptoms was recorded month by month for four consecutive years. A total of 420 patients with UC and 142 patients with CD were included. There was monthly seasonality ($p=0.028$) in symptomatic onset in December and January for UC but not for CD. It was found that environmental agents with known seasonality can be of importance for the seasonal variations of disease onset in UC.

(Gut 1996; 38: 376-378)

Keywords: Crohn's disease, aetiology, seasonality, ulcerative colitis.

Seasonal variations in the onset or relapse of chronic diseases such as inflammatory bowel disease (IBD) have been studied, with conflicting results.¹⁻¹² Most of the studies have dealt with relapses,³⁻⁹ but there are also a few analysing seasonal variations in the onset of disease.^{1,2,4} All the studies have used retrospectively assembled data or hospital admission, however, which may have lead to a bias in the results.

In three retrospective studies^{1,2,4} dealing with the symptomatic onset of ulcerative colitis (UC), seasonal variation in the onset was reported in two with a peak in December⁴ and from August to January.² In the third study,¹ no seasonality was found.

This study was designed to investigate whether there were seasonal variations in the onset of symptoms in patients with UC and Crohn's disease (CD). The patients were recruited from an ongoing study of incidence and the onset of symptoms was recorded for each month over four consecutive years of registration.

Methods

In a prospective incidence study of IBD in south eastern Norway, the onset of disease specific symptoms was registered in a standardised manner.¹³ The following symptoms were selected as being the most indicative: diarrhoea with blood, mucus or pus in the stool, abdominal pain, fever, and weight loss. Interviews and clinical examinations were carried out by gastroenterologists according to a standardised clinical registration form. The month of onset of disease specific symptoms was determined by mean of a standardised questionnaire at the first consultation with the specialist.

To obtain the most accurate time of onset of symptoms, only UC and CD patients with a disease history of 12 months or less were included. In cases where an enteric infection was the suspected cause of IBD symptoms, only those with negative stool cultures and serological tests were included in the study. In addition, and before inclusion in the study, the diagnosis of IBD was verified in every case one year after the initial examination. During the period of four years from 1 January 1990 to 31 December 1993, a total of 663 cases of IBD were registered with a disease duration of 12 months or less at the time of diagnosis. Of these patients, 75 were classified as indeterminate colitis and were excluded from the study. The study population comprised 434 patients with the diagnosis of UC and 154 patients with CD. Of these, 14 patients with UC and 12 patients with CD were not eligible for inclusion in the statistical evaluation because of uncertainty about the month of disease onset. Table I shows the clinical characteristics of the patients.

The study was approved by the regional ethics committee and confidentiality of records was maintained according to the guidelines issued by the health authorities.

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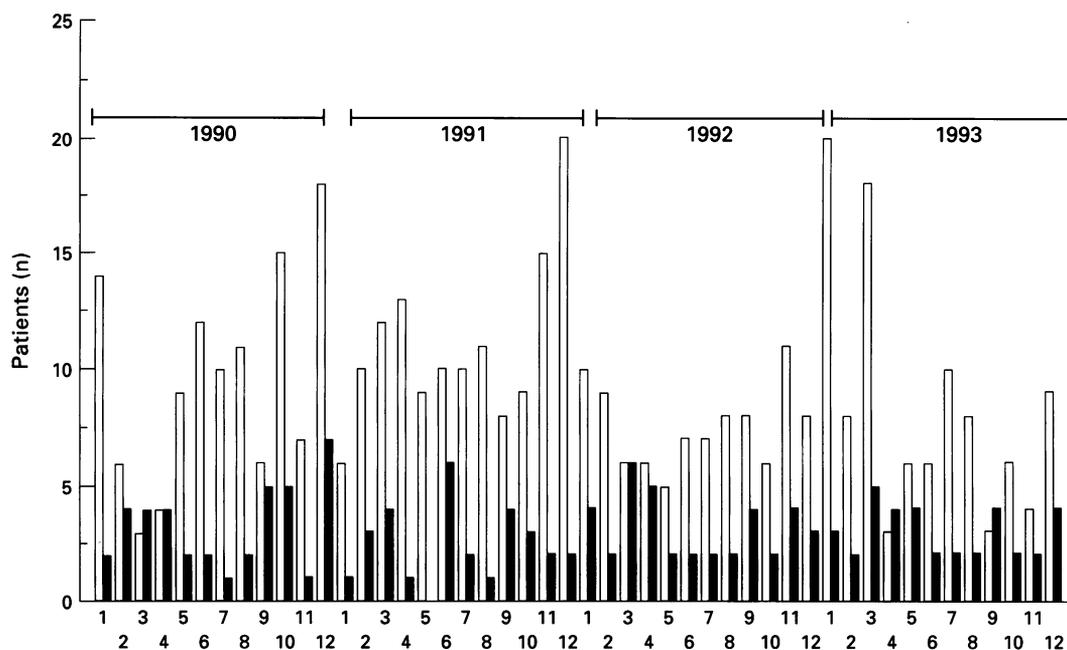
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TABLE I Clinical characteristics of ulcerative colitis (UC) and Crohn's disease (CD) patients with symptom duration of 12 months or less

	Ulcerative colitis	Crohn's disease
Number	420	142
Sex (M:F)	225:195	71:75
Age*	38 (28-56)	29 (22-44)
Disease extent in UC		
Proctitis	122 (29%)	
Left sided colitis	143 (34%)	
Extensive colitis	155 (37%)	
Disease extent in CD		
Large bowel		64 (45%)
Large and small bowel		44 (31%)
Small bowel		34 (24%)
Disease duration†	3.0 (2-5)	4.0 (2-6)
Symptoms‡ (%)		
Abdominal pain	44	79
Blood in stools	91	47
Diarrhoea	81	73
Mucus/pus in stools	73	48
Weight loss	30	58
Fever	15	28

*In years, median and interquartile range (IQR), †in months, median and IQR, ‡percentage of patients in each group.



Number of patients in each month in the 4 years

Numbers of patients with symptomatic onset of disease by month over a four year period. There were 420 cases of ulcerative colitis (□) and 142 cases of Crohn's disease (■).

Statistics

To test whether there was heterogeneity between the different months – that is, to test whether any significant departure from a uniform distribution had occurred – we used a χ^2 test taking into account the differences in the number of days in the months. In a second analysis testing for the presence of seasonality, we used Edward's test for a 12 month period.² This also tests the hypothesis that the frequencies follow a sinusoidal curve for a period of 12 months.

Results

The Figure shows the distribution of symptomatic onset of disease each month over four years. Table II shows the observed and expected frequencies of disease onset per month, taking into account the difference in number of days in each month. As regards the heterogeneity in UC, there was a significant

departure from a uniform distribution ($\chi^2_{(11df)}=21.6, p=0.028$) and Edward's test showed a seasonal pattern, with a peak at the end of December ($p=0.028$). In CD neither heterogeneity ($\chi^2_{(11df)}=14.6, p=0.200$), nor seasonal variations ($p=0.22$) were found.

Discussion

In patients with IBD, a broad variation is generally seen in the duration of symptoms before the disease is diagnosed. The date of the onset of symptoms or the first episode can be fairly difficult to determine, especially in the patients with a long disease history. Furthermore, data from retrospective studies are less reliable as regards the determination of the time of onset of IBD. To increase the reliability of this study, only cases with a symptom duration of 12 months or less were included. Thus the median duration of symptoms for both UC and CD was fairly short (Table I), and the determination of disease onset was considered to be reliable.

In prospective incidence studies of IBD, the inclusion of an accumulation of previously undiagnosed cases may cause a drop in the length of the disease duration, which may give an impression of seasonality. In this study, the median disease duration remained stable in UC (three months) and CD (four months) throughout the four years of registration, which suggests that the results do not reflect prevalence.

Weight loss initially affected 30% of UC and 58% of CD patients (Table I). It is difficult to determine the onset of weight loss, but in this survey only 2% of the patients claimed that weight loss was the only symptom leading to investigation for IBD.

Including cases with a sudden onset, or restricting the material to patients who could

TABLE II Observed versus expected monthly frequency of onset of symptoms in 420 patients with ulcerative colitis including proctitis, and 142 patients with Crohn's disease during four consecutive years of registration

	Onset of symptoms in patients with			
	Ulcerative colitis		Crohn's disease	
	Observed	Expected	Observed	Expected
January	48	35.7	10	12.0
February	31	32.0	11	10.8
March	37	35.7	19	12.0
April	26	34.5	14	11.8
May	27	35.7	8	12.0
June	33	34.5	12	11.8
July	36	35.7	7	12.0
August	36	35.7	7	12.0
September	22	34.5	17	11.8
October	35	35.7	12	12.0
November	36	34.5	9	11.8
December	53	35.7	16	12.0
χ^2_{11df}	21.6		14.6	
p Value	0.028		0.200	

specify the onset of symptoms with a high degree of precision would have skewed the material by including more patients with enteric infections as an exogenic factor precipitating IBD symptoms.¹⁴

Studies of factors that may induce the onset of UC and CD are surprisingly few.^{1 2 4} Various infectious agents have been proposed as possible aetiological factors, mainly for CD, but the empirical evidence is inconclusive.^{4 6 10 15-18} For example, measles has recently been suggested as a perinatal exposure factor,¹⁷ although other authors such as Sloan¹⁹ have found that exposure later in life precedes the onset of symptoms. Measles vaccination has been in place in Norway since 1974, however, and therefore there were no measles epidemics in Norway during the study period. Upper respiratory tract infections, bacterial enteric infections, and increased intake of analgesics, non-steroidal anti-inflammatory drugs and antibiotics have been implicated in disease relapse.^{4 6 7 10} Other reports have found no evidence of specific microbial agents in the pathogenesis of IBD, but conclude that concurrent infections, travelling abroad or the taking of antibiotics are intervening factors that may change the natural onset or precipitate or activate a latent IBD.^{14 16 18 19}

In this study seasonal variation in the onset of symptoms was found only in UC. This finding was based on the exceedingly high occurrence of symptoms in December and January, and on the lower frequency than expected in April and May. As upper respiratory tract infections have been associated with relapses in UC and CD,^{4 6 16 19} and as in Norway, both colds and upper respiratory tract infections show a seasonal distribution, with higher frequencies in the winter, the results of this study support the hypothesis that the onset of UC is precipitated by pathogens with known seasonality such as in upper respiratory tract infections. Increased use of antibiotics in the winter period in Norway (personal communication, The Norwegian Medicines Control Authority) could also support that the use of this drug could precipitate or activate a latent IBD.

The hypothesis that enteric infections can precipitate the onset of disease is not supported by these findings, as such infections are most common in Norwegians after holidays abroad during the summer. The fact that negative stool cultures and serological tests were a requirement for inclusion in the study, also means that such an association is unlikely.

In this study the numbers of UC patients each month seem to have been sufficient to obtain valid data. The comparatively smaller number of CD patients for each month, however, must be interpreted with caution, as a seasonality similar to that for UC cannot be ruled out.

In conclusion, the prospective registration of seasonal variations in the symptomatic onset in IBD showed seasonality in UC but not in CD. Factors related to climate may be at least partly responsible for the seasonal variation and the high incidence of UC found in Norway. Accordingly, pathogens with seasonal fluctuations may be of crucial importance for the occurrence of IBD. These findings need to be further investigated.

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