

# Observations on the Epidemiology and Colonoscopic features of Chronic Ulcerative Colitis in Maltese patients

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## ABSTRACT

A retrospective 2 year analysis of the endoscopic and histologic records of 34 Maltese patients with chronic ulcerative colitis is reported. The observed incidence of this condition in Malta is 1.9 per 100,000 per year. It is estimated that the present prevalence of the disease is 50 to 75 per 100,000 population.

Colonoscopic findings were used to determine the extent and severity of chronic ulcerative colitis. Nine patients (26.5%) showed signs of proctosigmoiditis; seventeen patients (50.0%) had inflammation extending to the splenic flexure (left-sided colitis) and eight patients (23.5%) had more extensive disease. These figures are compared to observations in published series from other population-based studies.

Non-specific histopathological features such as mononuclear cell infiltration of the mucosa were reported in 88.5% of biopsies but more characteristic abnormalities, such as crypt abscesses and goblet cell mucin depletion were less commonly documented.

These findings confirm the usefulness of endoscopy in the diagnosis and assessment of the extent and severity of inflammatory bowel disease. The data also provide a basis for the development of future prospective studies, and the establishment of a centralised, multidisciplinary inflammatory bowel disease clinic in Malta.

## INTRODUCTION

A new era in the investigation of colonic diseases began in 1970 with the introduction of flexible fiberoptic colonoscopes. The usefulness of this investigation has been verified in many previous studies (1,2). In Malta, the utilisation of this technique became commonplace in 1985, when an Endoscopy Unit was

established and a Medical Gastroenterology Unit provided a consultative colonoscopy service for identification and treatment of colonic problems such as rectal bleeding (3). Another common requirement in gastroenterologic practice in Malta is the assessment of the extent and severity of colitis in patients with inflammatory bowel disease. This is a critical issue in selecting the optimal treatment of patients with these disorders (4).

There is very limited information concerning the epidemiology of inflammatory bowel disease in Malta. The ability to identify index cases in a population that is easily accessible through a unique endoscopic facility in Malta has provided the opportunity to gain preliminary insights into questions of epidemiologic importance. Thus, in a previous study Cachia and Camilleri (5) reported a reliable estimate of the prevalence of Crohn's disease in Malta.

Understanding the epidemiology of inflammatory bowel disease, and particularly the more common condition of chronic ulcerative colitis, has important practical implications relevant to the provision of subspecialty expertise, diagnostic methods, organisation of follow-up, optimisation of treatment and establishment of joint medico-surgical consultations.

The aim of this retrospective study is to describe some aspects of the epidemiology, endoscopic and histologic features of a series of 34 Maltese patients with chronic ulcerative colitis and proctosigmoiditis who underwent colonoscopy between July 1987 and July 1989.

## MATERIALS AND METHODS

A. Selection of patients: The endoscopic and histologic records of 277 consecutive patients undergoing colonoscopy were reviewed. The

diagnosis of chronic ulcerative colitis was established in 34 patients, based on typical findings on history, rigid sigmoidoscopy and/or barium enema, colonoscopy and histology of mucosal biopsies.

B. Endoscopy and biopsy: Forty-five colonoscopies were performed by the author using an Olympus CFIT10L fiberoptic colonoscope (27 cases) or an Olympus ITS2 flexible sigmoidoscope (18 cases). Bowel preparation consisted either of sennoside 2 tablets, or sodium picosulphate 2 sachets, followed by 200 mls of 10% mannitol and two litres of water flavoured to taste. Sedation was achieved using intravenous midazolam 5-10mg, pethidine 25-75mg and metoclopramide 10mg. An attempt was made to reach the caecum or splenic flexure in all cases depending on the instrument available at the time of examination. This was achieved in 85% of cases (23 of 27 colonoscopies and 14 of 18 flexible sigmoidoscopies). Whenever endoscopic examination of the colon was incomplete (i.e. the entire colon was not examined), normal mucosa was visualised and biopsied beyond the segment of inflamed colon. Hence the extent of colonic inflammation could be defined macroscopically and microscopically in all cases.

In 10 patients, biopsies were taken at multiple colonic sites in a standardised manner (i.e. caecum, transverse colon, descending colon and rectosigmoid), irrespective of the level of visual demarcation of

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normal from abnormal mucosa. Otherwise, representative mucosal biopsies were taken from segments that appeared abnormal as well as from macroscopically normal mucosa. All biopsies were assessed by routine histology using light microscopy of haematoxylin and eosins stained sections.

C. Assessment of extent and severity of disease: Patients were grouped according to the extent of inflammation following endoscopic and histologic assessment. The extent of colonic involvement was classified as:

1. Proctosigmoiditis, i.e. is inflammatory mucosal changes confined to the distal 25 cm of sigmoid colon and rectum.
2. Left-sided colitis, i.e. inflammation extending above 25 cm from the anal verge, but not beyond the splenic flexure.
3. Proximal colitis when inflammation involved colon proximal to the splenic flexure.

The endoscopic features used in the macroscopic grading of inflammation were (4):

- a) loss of vascular pattern, diffuse erythema and mucosal oedema as characteristic of mild changes;
- b) contact haemorrhage, friability and granularity as indicators of moderate inflammatory activity;
- c) frank ulceration, inflammatory pseudopolyps or surface mucopus as features of severe inflammation.

The histopathology reports were retrospectively reviewed and the following findings were noted:

- i) presence of mucosal ulceration;
  - ii) crypt abscess formation;
  - iii) goblet cell mucin depletion;
  - iv) acute and chronic inflammation, based on mucosal infiltration with polymorphonuclear and mononuclear cells respectively.
- Incomplete biopsy reports which did not include sufficient details were excluded from analysis (n=4).

## RESULTS

A. Indications for endoscopy: A total of 42 procedures were performed on 34 patients for one or more of the following indications:

1. Differential diagnosis of diarrhoea

with or without rectal bleeding (n=19);

2. Assessment of the extent and severity of chronic ulcerative colitis at the time of first presentation, or after relapse in patients with known disease (n=14);

3. Surveillance for carcinoma (n=8);

4. Assessment of a stricture reported on barium enema in 1 patient with known chronic ulcerative colitis.

Repeat endoscopy was usually indicated for reassessment of clinical relapse of disease or for follow-up of therapeutic efficacy.

B. Complications: Significant pain that prevented completion of examination was noted in 7 patients. No major complications such as bleeding or perforation were observed in this series.

C. Colonoscopic and histologic findings: The number of patients in each group and their histologic and endoscopic features are shown in table 1. In the subgroup of the newly diagnosed 13 patients (i.e. with onset of disease during the study period), 8 had inflammation limited to the distal 25cm of rectum and colon, 3 had left-sided colitis and 2 were found to have total colonic involvement.

Mucosal biopsy reports were available in 30 of 34 patients and were sufficiently detailed to allow identification of the specific histological features (see table 1) outlined in the Methods section in 26 patients. Of the other 4 patients, 2 had chronic ulcerative colitis which was previously well documented on endoscopy and biopsy. In this study, colonoscopy revealed features consistent with chronic ulcerative colitis such as loss of haustral pattern and pseudopolyp formation in these 2 patients. The remaining 2 patients without detailed histological reports were newly diagnosed cases of proctosigmoiditis. The diagnosis was based on typical clinical features (recurrent bloody diarrhoea), positive radiologic findings and characteristic colonoscopic appearances.

D. Anthropometric data of patients with chronic ulcerative colitis: The age distribution of the whole group of 34 patients with chronic ulcerative colitis ranges between 12 and 70 years (mean 38.8 years). Thirteen

patients (6 males and 7 females) were diagnosed at the time of colonoscopy (mean age 38.2 years) whereas 21 patients had previously documented disease. Figure 1 shows the bimodal distribution of ages of the whole group with the two peaks showing a mean age of 19.8 years for the younger population and 48.6 years for the older population. The male to female ratio is one (17 males and 17 females).

E. Incidence of chronic ulcerative colitis: Based on the finding of 12 new patients in a 2 year study, the mean incidence of chronic ulcerative colitis is 1.9 per 100,000 per year (calculated on the population of Malta in 1985 as 340,907 [6]).

## DISCUSSION

This paper is the first collection of endoscopic and histologic observations of chronic ulcerative colitis in Maltese patients. Previous reports on local descriptions of inflammatory bowel disease include a study of the epidemiology and clinical features of Crohn's disease (5) and a review of the use of colonoscopy for investigation of rectal bleeding (3). In the latter study, 14 out of 94 patients (14.9%) were found to have inflammatory bowel disease. In the present study, a first attempt is made to calculate the incidence of chronic ulcerative colitis in Maltese patients.

The indications for endoscopy in this group of patients are comparable to those of other series (7). Colonoscopy permitted a clear evaluation of disease extent. The largest number of patients in this series had left-sided colitis (50%). An approximately equal number had either proctosigmoiditis (26.6%) or extensive, proximal colitis (23.5%). These figures are very similar to those reported in a Jewish population-based study reported from Tel Aviv (8) in which the data were derived from radiological examination (table 2). By comparison, the relative frequencies of the extent of disease in the Maltese and Jewish series are markedly different from those in another population-based study of patients in Rochester, Minnesota (9). The significance of these differences requires further exploration in a larger, more representative sample of Maltese patients in future

prospective studies.

Detailed biopsy reports were available in the majority of patients studied. Chronic inflammatory cell infiltration was most often reported in these biopsies (88.5%) but more specific histological features of chronic ulcerative colitis such as goblet cell mucin depletion, crypt abscess formation and acute inflammatory infiltrates were less frequently noted, each being present in 57.7% of biopsies. This suggests that despite availability of multiple colonic biopsies, general histopathologists may have some difficulty in distinguishing between ulcerative colitis and "non-specific colitis" (manifested by a chronic inflammatory cell infiltrate) on microscopic examination alone (10). Indeed, it is well recognised that while many features of inflammatory bowel disease are characteristic, none are pathognomonic. Well defined criteria, such as those suggested by Morson and colleagues (11,12) are useful in improving the sensitivity and specificity of histological diagnosis, but all clinical and investigational data are essential in evaluating the significance of histopathological changes apparent in colorectal biopsies (13). In future, multidisciplinary collaboration would allow better definition and management of this common condition.

Histologic assessment of disease activity is also very difficult to quantitate. A grading system of histological severity could not be utilised in this study owing to its retrospective nature, interobserver variation between different pathologists and the lack of standardisation and completeness of biopsy reports. Histologic scoring systems (14) contribute significantly to the use of mucosal biopsy specimens as the gold standard for the assessment of disease activity in inflammatory bowel disease.

The incidence of chronic ulcerative colitis calculated from this preliminary study is comparable to that seen in other European and North American studies. Similarly, age and sex distribution conform with the data in the literature. The average age of 38.8 years is similar to the mean of 34 years in a series of patients studied by Gabrielsson et

al in Sweden (15), and a bimodal distribution with peaks in the third and sixth decades can be distinguished in the Maltese group as in the Oxford study (16). Reports from Copenhagen and Baltimore (17,18) also noted a relatively high incidence of chronic ulcerative colitis after the age of 50 years, and this is confirmed by our experience in Malta.

Although this group of patients does not include all cases of chronic ulcerative colitis presenting between July 1987 and July 1989, it is interesting to note that the observed mean incidence rate of 1.9 per 100,000 population per year is identical to that reported from Bologna (19). This figure is likely to be a conservative estimate of the true incidence of chronic ulcerative colitis in Malta because this study did not sample all patients referred to St. Luke's Hospital with this condition. One might argue (on the basis of the usually quoted ratio of chronic ulcerative colitis being two to three times as common as Crohn's disease in various studies [20]) that the true incidence of this disease in Malta should be 4.2 to 6.3 per 100,000 per year. This calculation is based on the documented incidence of Crohn's disease in Malta of 2.1 per 100,000 per year (5). In contrast to the approximate estimate possible in the present study, the figure of 2.1 per 100,000 for Crohn's disease is likely to be accurate in view of the prospective nature of the study, and the rarity of the diagnosis of Crohn's disease in Malta prior to 1985, suggesting that the new expertise of a gastroenterologic service had attracted all potential patients for evaluation. This observation is, in fact, borne out by considering the length of patients' illnesses prior to diagnosis of Crohn's disease in the series of Cachia and Camilleri (5).

The prevalence of chronic ulcerative colitis in Malta remains unknown. In a number of communities where population-based studies have been performed, the average ratio between prevalence and incidence is 10 to 15. Assuming an incidence of 5 per 100,000 per year (see above), it is reasonable to speculate that the prevalence of chronic ulcerative colitis in Malta is 50 to 75 per 100,000; that is, there are probably 170 to 250 patients with this

condition on the Maltese Islands. However, prospective longitudinal studies are necessary to accurately answer such epidemiologic questions. These data emphasise the need to establish a centralised inflammatory bowel disease clinic in Malta and to start prospective studies of this common condition with a view to standardising diagnosis and treatment, and commencing cancer surveillance programmes.

In conclusion, this report has provided an opportunity to estimate the incidence and prevalence of chronic ulcerative colitis in Malta and confirms the usefulness and safety of colonoscopy (3) in the evaluation of colonic disease in Maltese patients.

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**ACKNOWLEDGEMENTS:** I wish to thank Prof. F.F. Fenech and the Consultant Medical and Surgical Staff at St. Luke's Hospital for referring patients for evaluation. It is also a pleasure to record the technical expertise and the excellent care of patients provided by the Endoscopy Unit Staff during these studies. This effort owes much to the training and guidance of the author by Dr. Michael Camilleri.

|                            | PROCTO-SIGMOIDITIS | LEFT-SIDED COLITIS | PROXIMAL COLITIS | TOTAL        |
|----------------------------|--------------------|--------------------|------------------|--------------|
| <b>PATIENTS:</b>           |                    |                    |                  |              |
| n                          | 9(26.5%)           | 17(50%)            | 8(23.5%)         | 34           |
| Males                      | 6(66.7%)           | 7(41.2%)           | 4(50.0%)         | 17           |
| Females                    | 3(33.3%)           | 10(58.8%)          | 4(50.0%)         | 17           |
| Mean age (y)*              | 43.9               | 40.0               | 38.8             |              |
| Age range (y)*             | 26 - 57            | 12 - 70            | 12 - 53          |              |
| <b>HISTOLOGIC FEATURES</b> |                    |                    |                  | <b>TOTAL</b> |
| Biopsies (n)               | 5                  | 14                 | 7                | 26           |
| Mucosal ulceration         | 2                  | 5                  | 2                | 9(34.6%)     |
| Crypt abscesses            | 4                  | 7                  | 4                | 15(57.7%)    |
| Goblet cell depletion      | 4                  | 6                  | 5                | 15(57.7%)    |
| Inflammation: acute        | 3                  | 8                  | 4                | 15(57.7%)    |
| chronic                    | 4                  | 13                 | 6                | 23(88.5%)    |
| <b>ENDOSCOPIC GRADE</b>    |                    |                    |                  | <b>TOTAL</b> |
| Mild                       | 3                  | 5                  | 3                | 11(32.4%)    |
| Moderate                   | 3                  | 5                  | 1                | 9(26.5%)     |
| Severe                     | 3                  | 7                  | 4                | 14(41.1%)    |
| *years.                    |                    |                    |                  |              |

TABLE 1:

Anthropometric, histologic and endoscopic data of patients with chronic ulcerative colitis by disease location.

## POPULATION

## EXTENT OF DISEASE

|                          | DIAGNOSTIC<br>METHOD | PROCTO-<br>SIGMOIDITIS | LEFT-SIDED<br>COLITIS | PROXIM<br>COLITIS |
|--------------------------|----------------------|------------------------|-----------------------|-------------------|
| (n = number of patients) |                      |                        |                       |                   |
| MALTA<br>(n=34)          | Endoscopy            | 26.5%                  | 50.0%                 | 23.5%             |
| MINNESOTA<br>(n=138)     | Radiology            | 48.6%                  | 15.2%                 | 36.2%             |
| ISRAEL<br>(n=155)        | Radiology            | 31.0%                  | 49.7%                 | 19.3%             |

TABLE 2

*Comparison of data from Maltese patients with published reports on chronic ulcerative colitis patients in other populations.*

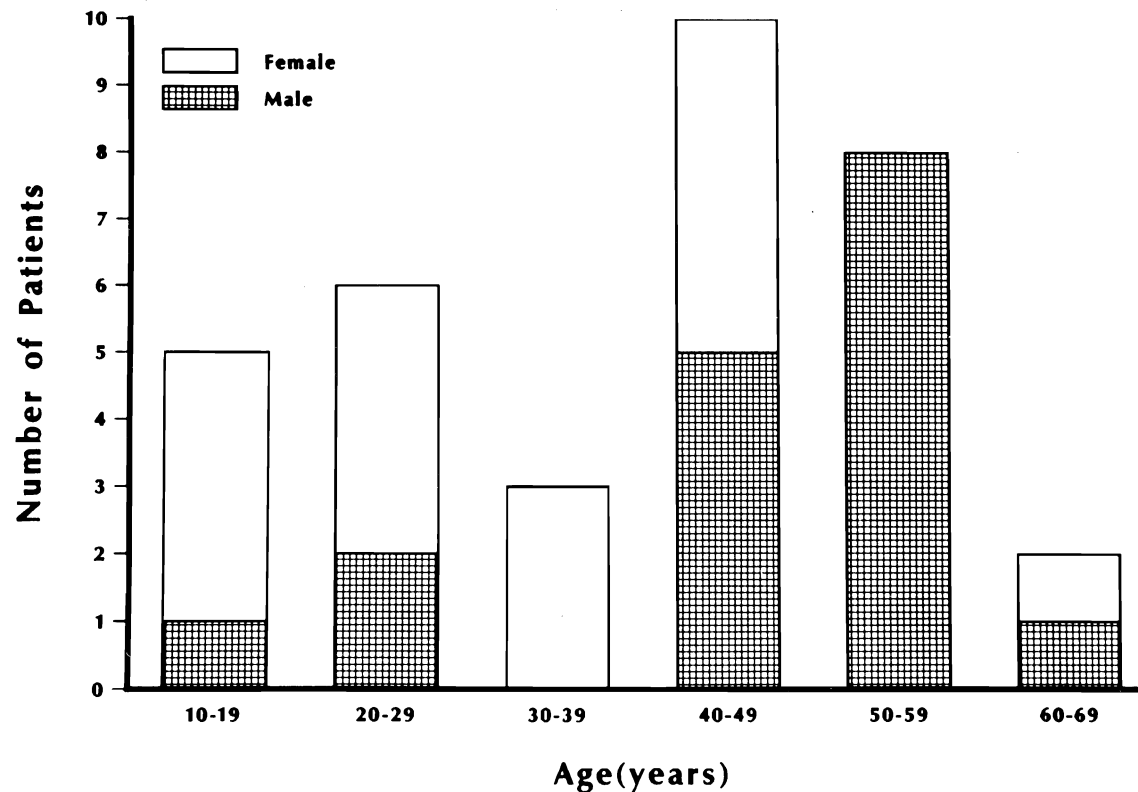


Figure 1:

*Frequency distribution of the ages of 34 Maltese patients with chronic ulcerative colitis.*

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