High Incidence of Crohn’s Disease in Canterbury, New Zealand: Results of an Epidemiologic Study

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Background: Inflammatory bowel disease (IBD) has increased exponentially in industrialized nations over the last 50 years. Previous New Zealand studies have shown that IBD is less common than in other countries; however, clinical observations suggested a high incidence and prevalence of IBD in Canterbury, particularly Crohn’s disease (CD).

Aim: This study aimed to determine the descriptive epidemiology of IBD in Canterbury.

Methods: Canterbury IBD patients, recruited using multiple strategies, gave informed consent, permission for clinical record review, completed a questionnaire, and were bled for DNA extraction as part of the Canterbury IBD Project. Cases were confirmed using standard criteria, and completeness of recruitment was validated using capture-recapture methods. Demographic and phenotypic data were extracted from case notes. One thousand four hundred twenty patients (715 CD, 668 ulcerative colitis [UC]) were recruited (>91% of Canterbury IBD patients).

Results: In 2004, age-standardized (World Health Organization World Standard Population) IBD, CD, and UC incidence rates were 25.2, 16.5, and 7.6/100,000/year, respectively. The IBD, CD, and UC point prevalences on 1 June, 2005 were 308.3, 155.2, and 145.0/100,000, respectively. CD patients were more likely than UC patients to be female (61.4% vs. 47.1%) and to be younger (median age, 39.9 years vs. 43.7 years). The percent of IBD patients who were white was 97.5%.

Conclusion: IBD is at least as common in Canterbury as in other western regions. CD incidence and prevalence are amongst the highest ever reported and are higher than for UC. IBD population characteristics are otherwise similar to other countries. The Canterbury IBD Project will be a valuable tool for future population-based IBD epidemiology and genetics research.

Key Words: inflammatory bowel disease, ulcerative colitis, Crohn’s disease, New Zealand, epidemiology

The inflammatory bowel diseases (IBD) Crohn’s disease (CD), ulcerative colitis (UC), and indeterminate colitis (IC) are increasingly significant health problems worldwide. Longitudinal studies over the last 50 years have shown an increasing incidence of UC first, followed by rapid rises in the incidence of CD.1–9 In some regions, the incidence of CD is now greater than that of UC, although in some areas, the incidence of both conditions is now stabilizing.10,11 Causes for the rapid changes in IBD incidence are elusive. Although advances have been made in understanding genetic factors that increase susceptibility to IBD, environmental factors that are likely to be the cause of this increase in incidence are yet to be identified.

There has been a dearth of population-based epidemiologic studies from the southern hemisphere. Wright and colleagues12 described the epidemiology of IBD in Cape Town, South Africa in 1986, although the methods of case identification used may have lead to incomplete case ascertainment. There have been three IBD epidemiologic studies performed previously in New Zealand, but all have been hospital based, which may have led to falsely low incidence and prevalence figures.13–15 Recent outpatient data from Christchurch hospital suggested that there has been an increase in the incidence and prevalence of IBD in Canterbury. We aimed to perform a definitive study of the descriptive epidemiology of IBD in Canterbury, New Zealand, to define the magnitude of IBD locally and allow comparison with regions worldwide.

SUBJECTS AND METHODS

Population

The Canterbury region was defined using the Canterbury District Health Board (CDHB) boundaries, shown in...
Over 90% of New Zealand has no such system. Although most geographic boundaries of Canterbury as defined by the Canterbury District Health Board and specific Territorial Local Authorities, the population and geographic area, and 74% of the population live within the Christchurch urban boundary. Over 90% of the population are of white ethnicity, following settlement by Europeans (predominantly from the United Kingdom and Ireland) beginning in the 1840s. The remainder of the population comprise Maori (7.2%), Pacific Islanders (1.8%), and people of other ethnicities, particularly from Asia. The Canterbury economy is centered on primary production, including agriculture, horticulture, and fishing, with an increasing emphasis on technology and development of a knowledge-based economy.

With regard to age distribution, 20.3% of the population is aged less than 20 years, whereas 13.8% are greater than 65 years of age. Population density in Christchurch is low compared with many cities, with apartment living uncommon.

**Case Identification and Diagnostic Criteria**

Unlike countries with universal health systems that have meticulous coding and diagnostic or therapeutic registry data, New Zealand has no such system. Although most New Zealand residents use the public health system, 14% have comprehensive private health insurance, and therefore patients attending both public and private clinics and hospitals need to be identified for epidemiologic studies. In addition, because of the relapsing-remitting nature of IBD, patients may be discharged from regular follow-up and could therefore be missed from recruitment. Therefore, to capture all patients, a multifaceted approach to case identification and recruitment is required.

This study was performed as one part of the Canterbury Inflammatory Bowel Disease Project, a large population-based project aimed at describing the epidemiology of IBD in the Canterbury region and to study the genetic and environmental determinants of IBD. Cases were recruited from multiple sources. Patients were approached in public and private clinics and inpatient wards to be recruited into the study. All gastroenterologists and surgeons in the region were informed of the study and its aims and referred patients directly into the study. These patients were classified as “medically referred”.

Members of patient support groups, such as the Crohn’s and colitis support group, were informed of the study and invited to participate. Advertisements were placed in the rooms of specialists and general practitioners (GPs) within Canterbury and in local newspapers. News reports concerning the study appeared on television stations and radio networks in Canterbury. Patients who presented for recruitment as a result of this approach were classified as “self referred”.

Finally, computer records from all clinics in Canterbury were screened using text searches for the words “Crohn”, “colitis”, “proctitis”, and for the trade and generic names of sulphasalasine and the 5-aminosalicylate drugs. Case notes were reviewed and letters mailed to patients from their physician inviting them to take part in the study. Patients who were recruited this way were classified as “invited”.

To validate the completeness of recruitment for the study, the computer records of two representative general practices were searched using the methods described above. The characteristics of the general practices were representative of the Canterbury population enrolled with a GP with regard to age, sex, and privately insured characteristics. IBD cases were identified and confirmed using the same diagnostic criteria as the cases. The observed percentage of IBD patients in the GP practices who were actually recruited into the study was used to determine the completeness of recruitment. In addition, the proportion of IBD patients in these general practices was extrapolated to the Canterbury population as a further estimate of the completeness of recruitment.

To help with recruitment of incident cases prospectively, gastroenterologists, surgeons, and GPs were informed of the study both by letter and meetings. The investigators were then informed about the patient, and their diagnosis and patient consent was obtained. Pathology reports from local laboratories were screened during 2004 to help confirm and identify further incident cases.
At recruitment into the study, subjects met with one of the investigators (RBG) and gave informed consent and permission to access their medical notes. At a later date, one of the investigators (RBG) or a trained research assistant examined the subject’s medical record to confirm the diagnosis and extract specific clinical information.

The diagnosis of IBD was confirmed according to recognized and accepted criteria. Other diagnoses were rigorously excluded. Participants (n = 47) who were unable to give informed consent, declined to participate, or did not live in Canterbury were not included in the study, as were participants who did not have IBD confirmed by standard criteria. If there was doubt as to the diagnosis or if insufficient data to confirm the diagnosis, the case was discussed with the patient’s clinician, and all available results were reviewed before a final decision on inclusion in the study. If there was still doubt concerning the diagnosis, then the patient was excluded. In addition to fulfilling these diagnostic criteria, all patients were phenotyped according to established classification systems. The study had ethical approval from the Canterbury Ethics Committee, and written informed consent was obtained from all subjects.

Analysis

Incidence rates were calculated for CD, UC, and IC for the period January 1, 2004 to December 31, 2005. Projected population data by age, sex, and ethnicity for Canterbury were obtained from the Department of Statistics. Annual incidence rates for 2004 for both sexes were calculated based on the number of patients diagnosed and the population size. Incidence rates were age standardized using the World Health Organization (WHO) Standard Population to allow comparison with other regions in the future. Exact binomial confidence intervals (CI) for the age-adjusted incidence rates were calculated because of the low numbers in some of the age groups. For age-specific prevalence rates, 95% CIs were calculated using the Poisson approximation. Prevalence was described as point prevalence on June 1, 2005.

RESULTS

Patient Recruitment

One thousand four hundred sixty-two IBD cases were initially recruited into the study. Three additional patients were not recruited because they were unable to give informed consent, and a further two patients actively declined to participate in the study. Forty-two patients were then excluded from the study because the diagnosis of IBD was not confirmed on review of clinical notes (17 irritable bowel syndrome, 7 diverticulitis, 4 ischemic colitis, 2 colorectal cancer, 2 solitary rectal ulcer, 2 nonsteroidal anti-inflammatory drug-associated enteropathy, 1 small bowel vasculitis, 1 lymphocytic colitis, 1 intestinal tuberculosis) or because the patient had IBD but was not resident in Canterbury (5). This left 1420 IBD patients recruited into the study.

Characteristics of Subjects Recruited by Different Methods

Patient characteristics are summarized in Table 1. A greater proportion of CD compared with UC patients were recruited at outpatient clinics or on medical wards, whereas UC patients were more likely to have been invited to take part in the study. Table 1 also shows that there were more

TABLE 1. Characteristics of Canterbury Inflammatory Bowel Disease (IBD) Cohort

<table>
<thead>
<tr>
<th>Recruitment Method</th>
<th>CD (%)</th>
<th>UC (%)</th>
<th>IC (%)</th>
<th>IBD (%)</th>
<th>Estimated Canterbury Population (2004)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medically referred</td>
<td>459 (64.2)</td>
<td>354 (53.0)</td>
<td>33 (89.2)</td>
<td>846 (59.6)</td>
<td></td>
</tr>
<tr>
<td>Self referred</td>
<td>168 (23.5)</td>
<td>129 (19.3)</td>
<td>1 (2.7)</td>
<td>298 (21.0)</td>
<td></td>
</tr>
<tr>
<td>Invited</td>
<td>88 (12.3)</td>
<td>185 (27.7)</td>
<td>3 (8.1)</td>
<td>276 (19.4)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>293 (41.0)</td>
<td>342 (51.2)</td>
<td>18 (48.7)</td>
<td>653 (46.0)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>422 (59.0)</td>
<td>326 (48.8)</td>
<td>19 (51.3)</td>
<td>767 (54.0)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maori</td>
<td>8 (1.1)</td>
<td>6 (0.9)</td>
<td>0</td>
<td>14 (1.0)</td>
<td>33,630 (7.3)</td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>8,292 (1.8)</td>
</tr>
<tr>
<td>Other</td>
<td>707 (98.9)</td>
<td>662 (99.1)</td>
<td>37 (100)</td>
<td>1,406 (99)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>715 (50.4)</td>
<td>668 (47.0)</td>
<td>37 (2.6)</td>
<td>1,420 (100)</td>
<td></td>
</tr>
</tbody>
</table>

CD = Crohn’s disease; UC = ulcerative colitis; IC = indeterminate colitis.
IBD Incidence

The incidence of IBD in Canterbury was determined prospectively between January 1, 2004 and December 31, 2004. Age-specific incidence rates (5 year age groups) by sex are shown in Figure 2. For 2004, the crude incidence rate for IBD per 100,000 was 25.2 (95% CI, 20.8–30.2), for CD 16.5 (95% CI, 13.0–20.4), for UC 7.6 (95% CI, 5.3–10.6), and for IC 1.1 (95% CI, 0.1–2.0). There is a peak of incidence for both CD and UC between 20 and 34 years of age. A further peak is seen for CD between the ages of 64 and 79. The age-specific incidence rates were standardized to the WHO World Standard Population Distribution. The age-standardized incidence in 2004 for IBD, CD, UC, and IC were 24.9 per 100,000, 16.3 per 100,000, 7.5 per 100,000, and 0.3 per 100,000, respectively.

IBD Prevalence

The point prevalence of IBD was determined on June 1, 2005. Figure 3 shows the age-specific prevalence by sex. The prevalence of IBD in Canterbury per 100,000 was 308.2 (95% CI, 292.2–324.3), for CD 155.2 (95% CI, 143.8–166.6), for UC 145.0 (95% CI, 134.0–156.0), and for IC 8.0 (95% CI, 5.4–10.6). Age-standardized (WHO Standard Population Distribution) prevalence per 100,000 was 274.3 for IBD, 145.3 for CD, 121.6 for UC, and 7.4 for IC. There is a rapid rise in IBD prevalence from the age of 15, women than men with CD, and both CD and UC were rare in Maori and Pacific Island people.

FIGURE 2. Age-specific incidence of inflammatory bowel disease (A), Crohn’s disease (B), and ulcerative colitis (C) in Canterbury in 2004.

FIGURE 3. Age-specific prevalence of inflammatory bowel disease (A), Crohn’s disease (B), and ulcerative colitis (C) in Canterbury in 2004.
peaking at the age of 34, and then remaining relatively stable. This reflects the early incidence peak shown in Figure 2.

There is also a rapid rise in CD prevalence, peaking between 25 and 39 years of age. This reflects the recent increase in the incidence of CD and the age distribution of those recently diagnosed with CD, shown in Figure 2. There are more women than men with CD in almost every age group. There is a slow rise in UC prevalence, peaking at the 60 to 65 year age group, with more men than women in the older age groups.

Validation of Prevalence Data Using GP Databases

The characteristics of the GP population used to validate recruitment into the prevalence study were similar to that of the Canterbury population, except that there were slightly more women (54% in the GP patient population compared with 50.8% in the Canterbury population), and the median age was slightly older (34 years in the GP population compared with 31 years in the Canterbury population).

Eighty-one of the GP patients were confirmed as having IBD. These came from a combined GP population of 23,976 patients, who comprised 5.2% of the Canterbury population. Interestingly 74 of the 81 (91.4%) patients had been recruited into the Canterbury IBD Project. This gives an estimated IBD prevalence of 335.7 per 100,000 (95% CI, 319.0–352.4 per 100,000), suggesting that our recruitment had been approximately 91% (one-tailed 95% CI > 86.2%).

Demographic Characteristics of Canterbury IBD Population

Figure 4A demonstrates the age of diagnosis for CD patients divided into male and female sexes. For the entire cohort, the peak age of diagnosis for CD patients was approximately 25 years, although a second smaller peak can be seen between 50 and 60 years. Figure 4B demonstrates the data for patients with UC. The peak age of diagnosis for UC patients is slightly later than that of CD, at 30 years, with no clear second peak. For CD, the median ages of diagnosis were 29 and 30 for males and females, respectively, whereas for UC, the median age of diagnosis were 38 and 35, respectively.

DISCUSSION

This is the first study to define comprehensively the descriptive epidemiology of IBD in a region of New Zealand. Previous studies have been hospital based, or described only CD or UC, or had significant methodologic problems. No previous study has prospectively assessed IBD incidence in New Zealand. Furthermore, this is one of only two population-based studies of the descriptive epidemiology of IBD performed in the southern hemisphere.

A multifaceted approach was used to recruit people in Canterbury who had incident and prevalent IBD cases in 2004, including referral from gastroenterologists, physicians, surgeons, and pediatricians, in addition to searching anatomic pathology reports, inpatient discharges, and outpatient letters from public and private clinics. This approach to recruitment has reduced many of the biases previously raised by other investigators. First, by combining self-referred, medically referred, and invited patients, underestimation of prevalence and incidence was reduced. This compares favorably with administrative databases that are often hospital based or not truly population based. Up to 80% of IBD patients in some series are never hospitalized; therefore, use of such databases will significantly underestimate prevalence. In addition, invited participants included those who had not seen their specialist for a long period of time (records were searched back for 15 years).

In some epidemiologic studies using health provider or administrative databases, patient records were not checked individually. This can lead to misclassification of non-IBD cases or exclusion of IBD cases, depending on the methods.
used.\textsuperscript{25} In this study, all patient records were checked individually, including anatomic pathology, radiology, and endoscopy reports in addition to patient letters, operation reports, and drug treatments. Established diagnostic criteria were used,\textsuperscript{19} and additional data on phenotype were also extracted. Others have used self-reported IBD diagnosis and compared this with established databases.\textsuperscript{11,26} Although this approach has the advantage of validating the self-referred patients, rigorous care must be taken to ensure this validation occurs. For example, in the present study, 380 people self referred for the study. Forty-five were excluded before they were recruited because IBD was ruled out after simple questioning. A further 37 were excluded later after review of their clinical notes when alternative diagnoses were found. Thus, 21.6\% of all those who self referred did not have IBD. The rigorous checking of clinical notes would have also avoided prevalent cases being misclassified as incident cases, minimizing misclassification in this study.

Recruitment of all prevalent IBD cases in Canterbury was more difficult than recruitment of incident cases. Although a multifaceted approach was used, an unknown number of patients did not take part in the study. By using the GP databases, it was estimated that over 91\% of people with IBD would have been included in the study, although there are a number of caveats on extrapolating from this general practice population. First, there were more women enrolled as patients in this GP population than expected (54\% vs. 50.8\%). There are more women than men in Canterbury with IBD, and therefore this may have led to an overestimation of IBD in Canterbury. In addition, 6\% of Cantabrians are not enrolled with a GP. It is more likely that people with a significant chronic medical condition (such as IBD) would be enrolled with a GP than those without such a condition. This could also lead to overestimation of IBD prevalence. Therefore, it can be assumed that at least 91\% of people in Canterbury with IBD were recruited into the study, suggesting that this is a true population-based cohort. In addition, the exclusion of five patients who were unable to or who did not wish to give informed consent will have led to an underestimation of IBD prevalence.

The crude incidence rates of 25.2 per 100,000 per year, 16.5 per 100,000 per year, and 7.6 per 100,000 per year for IBD, CD, and UC in Canterbury for 2004 are at the upper end of those described in Western countries previously. The highest incidence of CD reported in the medical literature is 15.6 per 100,000 person-years from Manitoba in Canada between 1987 and 1996.\textsuperscript{26} Therefore, Canterbury has the highest ever reported incidence of CD. However, this comparison may be misleading for a number of reasons. First, there have been few descriptive epidemiology IBD studies since 1996. Previous longitudinal epidemiologic studies show that the incidence of IBD is dynamic, and therefore comparison with old data may not be valid. Second, very few studies standardize their data using international standard populations to allow comparisons between populations. Although the Canterbury population is very close in age and sex structure to the Standard Population Distribution published by WHO, other populations may be significantly different.

The second striking finding from the present study is that there are significantly more people currently being diagnosed with CD than UC. Follow-up data from this cohort (not shown) suggests that the relative change of incidence between CD and UC has occurred over the last 10 years, during which time the incidence of UC has remained stable whereas that of CD has increased exponentially. A number of the epidemiologic studies performed recently have shown a similar phenomenon, particularly those from Northern France\textsuperscript{10} and Manitoba,\textsuperscript{11,26} although not to the same extent as in Canterbury. The causes for this change in IBD incidence are not clear, although the patterns of changing incidence for both UC and CD appear to be consistent with the patterns seen elsewhere. Environmental factors are most likely to be responsible for these observations, although an improved ability to diagnose CD because of patient and doctor awareness and improved technology such as wireless capsule endoscopy may also be implicated. It is important that IBD epidemiology is studied in other regions because comparison between populations (using age-standardized incidence rates) may give insights into IBD etiology, particularly with regard to environmental triggers.

Increasing CD incidence in Canterbury over the last 10 years has led to the prevalence of CD (155.2 per 100,000) being greater than that of UC (145.0 per 100,000). This is supported by the observation that the age-specific incidence and prevalence peaks for CD are very close together (Figs. 3B and 4B). Although prevalence data gives little insight into IBD etiology, the high overall prevalence in Canterbury (308.2 per 100,000) has important implications for providing medical care for IBD patients in Canterbury. IBD is a chronic disease, and patients require long-term medical supervision, including access to new investigations and treatments. The morbidity associated with this disease is significant. People who are young at diagnosis are often affected for long periods of time.

It is difficult to compare directly the prevalence of IBD in Canterbury with that from other countries or regions because of the paucity of recent prevalence data from elsewhere. However, a study of two national birth cohorts born in 1958 and 1970 in Britain allows some useful comparisons to be made.\textsuperscript{27} Ehlin and colleagues\textsuperscript{27} found a self-reported CD prevalence of 375 per 100 000 for a group of 30 year olds born in 1970 compared with a prevalence of 211 per 100 000 for the 1958 cohort when aged 30 years and 325 per 100,000 per year for the same cohort when aged 42 years. The prevalence from the 1970 cohort is similar to that for the 30 to 34 year age group in our study (336.6 per 100,000), although the age-specific prevalence at 42 years for the 1958 cohort is higher than that found in Canterbury (192.9 per 100,000).
The demographic characteristics of the Canterbury IBD population are similar to those published elsewhere, with respect to age at diagnosis and sex. First, there is a peak of diagnosis between 15 and 35 for both CD and UC. There is also a later peak, particularly for CD, between 65 and 74 years of age that is more prominent than described in many studies. However, the number of patients in these age groups is small, as reflected by the wide 95% CIs.

Most studies show more females than males with CD, as demonstrated in Figures 2B, 3B, and 4A, although males have a higher age-specific incidence of CD up until the age of 14 in this study, as has previously been shown elsewhere. Males have a higher age-specific prevalence of UC in the older age groups than females. This implies that environmental factors may have exerted differential effects on the risk of developing UC between males and females in the past, although it is difficult to explore this further without prospective collection of incidence data. Obviously, the role of hormonal factors (both endogenous and exogenous) need to be considered to explain these observations.

As with other epidemiologic studies of IBD from New Zealand, this study shows that IBD is rare in Maori and Pacific Islanders. It is difficult to know what, if any, genetic or environmental factors may protect these groups from IBD, and it will be interesting to observe whether IBD incidence increases rapidly in these groups as it has in other nonwhite populations. This also presents interesting opportunities for genetic admixture mapping studies.

Previous IBD epidemiology studies in New Zealand have suggested that IBD was less common in New Zealand than elsewhere. This is not the case in Canterbury, where the incidence and prevalence of CD are very high. It is possible that the high rates of IBD seen in Canterbury may be representative of New Zealand as a whole. However, ethnic and possibly undefined environmental factors are also likely to have a significant effect on rates throughout the New Zealand. This cohort provides a unique opportunity to study etiologic factors, particularly those of an environmental and genetic nature, in a population-based cohort.

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