ORIGINAL ARTICLE

The epidemiology and clinical characteristics of Crohn's disease in the Hong Kong Chinese population: experiences from a regional hospital

CME

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Objective To study the descriptive epidemiology and clinical profile of patients with Crohn's disease.

Design Retrospective study.

Setting Regional hospital, Hong Kong.

Patients Patients with Crohn's disease diagnosed between January 1991 and December 2006 inclusive.

Results Over the period studied, 27 Chinese patients were diagnosed with Crohn's disease in our hospital. Our hospital-based incidence and prevalence rate had increased more than 2- and 5-fold, respectively over that period. The mean age at diagnosis was 26 years and median duration of disease was 81 months. Most patients had ileocolonic disease (67%) followed by Crohn's colitis (22%) and ileal disease (11%); more patients had non-stricturing and non-penetrating disease (63%) than stricturing (15%) or penetrating disease (22%). Peri-anal disease occurred in 37% of our patients. At diagnosis, many of the patients (41%) had mild-moderate disease, but 30% each had moderate-severe and severe-fulminant disease. At the time of this study, 85% of the patients were in disease remission with medical treatment. However, 48% had undergone surgery for diagnosis or complications. No patient had developed colorectal cancer or died.

Conclusions The incidence and prevalence of Crohn's disease are increasing in the Chinese population. It usually affects young persons with a substantial proportion of patients presented with severe-fulminant disease. More epidemiological and clinical studies are needed for this emerging disease in Asian regions.

Introduction

Inflammatory bowel disease (IBD) was previously regarded as a disease of western countries. A number of studies showed that the incidence and prevalence of IBD were high in the United States, the United Kingdom, and Northern Europe,[1-3] whereas it was considered uncommon in Asian populations such as in Singapore, Malaysia, and Hong Kong.[4-6] However, a rising incidence and prevalence has been recently observed in Asian countries.[7-9] The reason for this trend could be improved physician awareness of the disease, improved access to medical care, and the development of effective diagnostic tools. On the other hand, strong epidemiological evidence suggests it might be related to the westernisation of lifestyle and changing eating habits, possibly relating to increasing affluence. For instance, first-generation Indian immigrants to the United Kingdom had a higher chance of developing IBD than people in India.[10,11] Also, young Asians born in Britain were at a significantly higher risk of developing IBD than indigenous Europeans.[12]

Crohn's disease (CD) is rare in Hong Kong, and is characterised by chronic inflammation, potentially involving any location in the alimentary tract. Although genetic, environmental, and immunological mechanisms have been postulated, its aetiology and exact pathogenesis remain unknown. The cost of medical and surgical therapy of CD is substantial and rising due to the advent of newer biological treatments.[13] Despite the rising occurrence and cost of treatment, data regarding the epidemiology of Chinese CD patients are not abundant. Although the clinical characteristics of CD in the Chinese

Key words
Crohn disease; Epidemiologic studies; Incidence; Prevalence

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population are well-described in the literature, the accounts are conflicting.[14-18] Experiences from the western countries may not be applicable to our local population. A better appreciation of these aspects can provide clues as to aetiological factors and the better allocation of resources for patient management. We therefore conducted a retrospective analysis of all CD patients in our centre, with the aim of determining the incidence, prevalence, and clinical characteristics of CD in our local Chinese community.

香港華裔人口中克羅恩病的流行病學和臨床特點：香港一所分區醫院的經驗

目的 檢視華裔克羅恩病患者群的描述性流行病學和臨床特點。

設計 回顧研究。

安排 分區醫院，香港。

患者 1991年1月至2006年12月診斷患上克羅恩病的病人。

結果 研究期內，醫院共診斷有27名華裔病人患上克羅恩病，院內發病率上升兩倍，而現患率更急升五倍。患者接受診斷時平均26歲，患病期中位數為81個月，大部份患者先患回結腸病（67%），繼發克羅恩結腸炎（22%）和回腸炎（11%），出現非特異性非透壁性病症性質的患者（63%）比特異性（15%）或透壁性（22%）的患者較多。37%病人患肛周疾病。接受診斷時，很多患者（41%）的病情屬微中度，但有30%是中重度，另30%是爆發性重症。研究期間，85%病人接受治療而病情正在減輕，不過其中因為診症或併發症而已接受手術的患者有48%。沒有病人患上結直腸癌，也無人死亡。

結論 克羅恩病的發病率和現患率在華裔人口中不斷上升，受影響的通常是年青人，其中相當大量患者出現爆發性重症。對於這種在亞洲區日見普遍的疾病，醫學界須進行更多流行病學和臨床研究。

Methods

All patients diagnosed to have CD in Tuen Mun Hospital from January 1991 to December 2006 inclusive were recruited for analysis. Patients were identified from their hospitalisation, ambulatory gastroenterology clinic, endoscopic and surgical procedure records. To verify completeness of case recruitment, our patient list was compared with that generated from Clinical Management System, a central computerised medical record system utilised by the Hong Kong Hospital Authority. Tuen Mun Hospital is a public regional hospital serving a population of 1 095 400 in the year 2006. Most (94.9%) of our population was ethnically Chinese.[19] Each public regional hospital in Hong Kong has a well-defined catchment area and referral system. Thus, primary care physicians from Tuen Mun and Yuen Long districts refer their gastroenterological patients to our specialist clinic for management.

The medical records, endoscopic, radiological, and histological results of all CD patients were reviewed. The following data were retrieved for analysis: (1) sex, (2) age at diagnosis, (3) duration of disease, (4) presenting symptoms, (5) duration of symptoms before diagnosis, (6) smoking status, (7) family history of IBD, (8) classification of CD, (9) activity of disease at diagnosis, (10) extra-intestinal manifestation, (11) treatment modalities, and (12) clinical outcomes. The number of new cases in each year from 1991 to 2006 was recorded to determine the incidence rate.

Classification of CD was performed according to the Montreal classification,[20] which groups subjects according to age at diagnosis (A1: ≤16 years; A2: 17-40 years; A3: >40 years), location of disease (L1: ileal; L2: colonic; L3: ileocolonic; L4: isolated upper disease), and disease behaviour (B1: non-stricturing, non-penetrating; B2: stricturing; B3: penetrating; p: peri-anal disease modifier). The activity of CD at diagnosis was classified clinically according to working definitions as: mild-moderate, moderate-severe, and severe-fulminant.[21]

Case ascertainment

A case of CD had to satisfy the internationally accepted Lennard-Jones criteria for diagnosis of IBD,[22] that depend on appropriate clinical, endoscopic, histopathological, and radiological findings. Typical features of CD included mucosal cobblestoning, linear ulcerations, skip lesions, transmural inflammation, epithelioid granuloma, stricture and fistula formation. Indeterminate colitis, infectious and other recognised causes of intestinal inflammation were carefully excluded by appropriate investigations. The diagnosis had to be present at least 6 months. We conducted a concurrent study on our patients with ulcerative colitis[23]; and by definition, an individual could not be counted in both studies.

Statistics

The crude prevalence rate of CD from 1991 to 2006 was calculated, using the total number of residents in our catchment area in that year as the denominator and the total number of patients with CD in that year as numerator. Crude incidence rates from 1991 to 2006 were calculated by using the total number of residents in that year as the denominator and the number of new cases of CD in that year as the numerator. The year of diagnosis of CD rather than the year of symptom onset was used to determine incidence, in order to avoid recall bias. Incidence and prevalence rates were expressed as the number

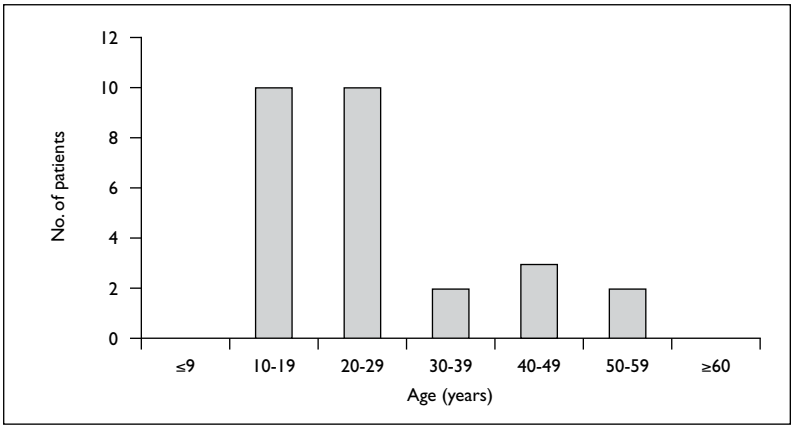

FIG 1. Age distribution at diagnosis of Crohn's disease

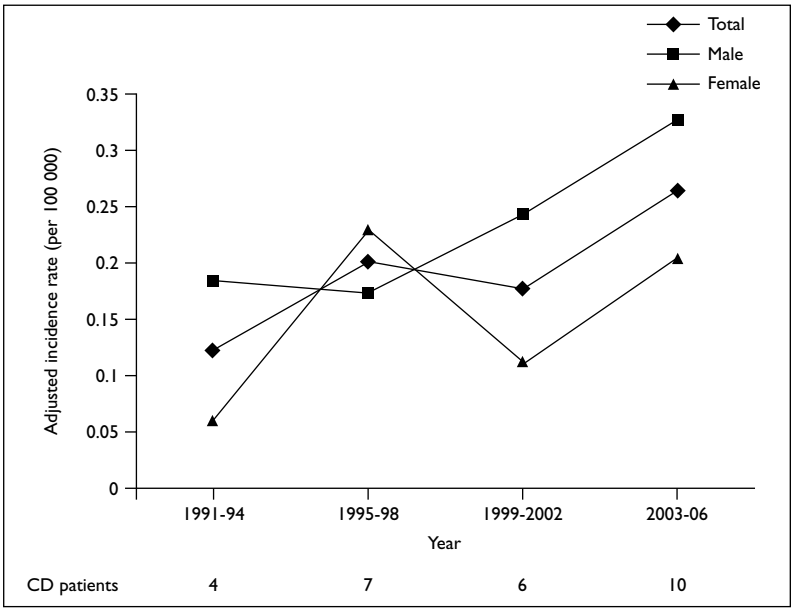

FIG 2. Age-adjusted incidence rate of Crohn's disease (CD) from 1991 to 2006
The total rate is sex- and age-adjusted. The numbers of newly diagnosed CD patients (all Chinese) in each period are shown

of patients per 100 000. Population figures in our catchment area in the years 1996, 2001, and 2006 were obtained from Census and Statistics Department of Hong Kong.[19] As recommended by the Census and Statistics Department, an annual increment rate of 1.8% from years 1996 to 2000 and 0.9% from years 2001 to 2006 was used to estimate the population size in the years intervening between censuses. An annual decrement rate of 1.8% was used to estimate population size from 1991 to 1995. To compare incidence and prevalence rates over time for an area with a changing population, adjustments were performed taking into account of age and sex, using the standard population for the year 1996.

Results

Demographics

From January 1991 to December 2006, 27 patients (16 males, 11 females) were diagnosed to have CD in our centre. All of them were ethnically Chinese. Their mean age at diagnosis was 26 years (range, 11-56 years) and their age distribution is shown in Figure 1. Two patients were current smokers, and the other 25 never smoked. Only one patient had a first-degree relative (younger brother) with confirmed CD. During the study period, no patient was reclassified between the two types of IBD.

Epidemiology

The crude incidence rate of CD increased more than 2-fold from 0.12 per 100 000 to 0.25 per 100 000 over the study period, whilst the crude prevalence rate increased more than 5-fold from 0.49 per 100 000 to 2.70 per 100 000. The corresponding rising temporal trends of age- and sex-adjusted incidence and prevalence rates are shown in Figures 2 and 3.

Clinical presentations

The median duration from symptom onset to diagnosis was 180 (range, 1-2520) days. The common presenting symptoms included abdominal pain (74%), diarrhoea (59%), per rectal bleeding (44%), fever (26%), weight loss (22%), and anaemia (19%). Other presentations included fistula-in-ano, recurrent oral aphthous ulcers, and extra-intestinal manifestations. Extra-intestinal manifestations were found in four patients (erythema nodosum 1, uveitis 1, sacroiliitis 1, and juvenile rheumatoid arthritis 1). Five (19%) patients presented as acute emergencies, which included two with active lower gastro-intestinal (GI) bleeding, two with intestinal obstruction, and one with ileal perforation. In all, 24 of the 27 patients underwent colonoscopy, the exceptions being the one with ileal perforation and the two with intestinal obstruction. Nine (33%) patients underwent upper endoscopy and 19 (70%) patients had barium meal and followed through studies. Although most (70%) patients were diagnosed based on endoscopic and radiological findings, in eight (30%) the diagnosis was confirmed after surgery.

Phenotypes

The disease phenotype was classified as non-stricturing and non-penetrating in 63% of the patients, stricturing in 15%, and penetrating in 22%. Ten (37%) patients had peri-anal disease, including anal fissure, fistula, and abscess. In 11% of the patients, the CD affected their terminal ileum, in 22% it was colonic and in 67% there was ileocolonic involvement

TABLE. Phenotypes of Crohn's disease patients according to the Montreal classification

Phenotype	No. of patients
Age at diagnosis (years)	
A1: ≤16	4 (15%)
A2: 17-40	20 (74%)
A3: >40	3 (11%)
Disease location	
L1: ileal	3 (11%)
L2: colonic	6 (22%)
L3: ileocolonic	18 (67%)
L4: isolated upper disease	0
Disease behaviour	
B1: non-stricturing, non-penetrating	17 (63%)
B2: stricturing	4 (15%)
B3: penetrating	6 (22%)
p: peri-anal disease modifier	10 (37%)

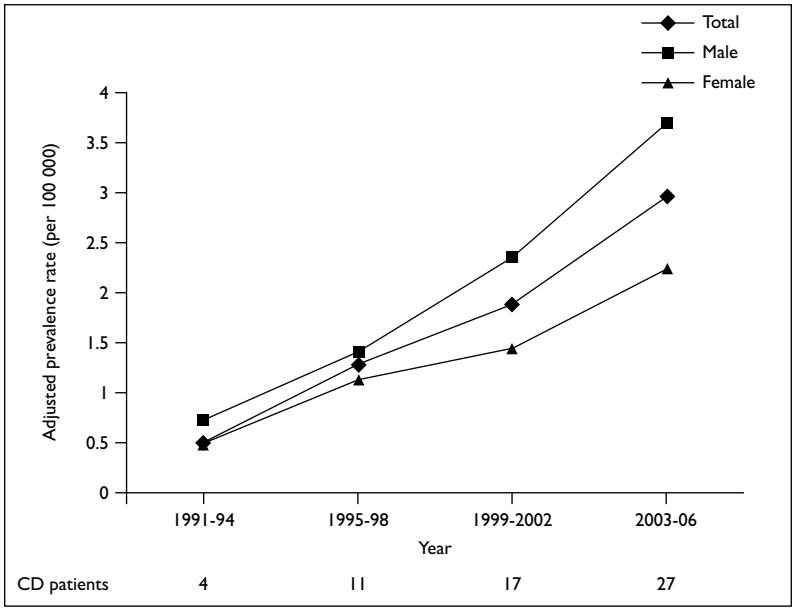

FIG 3. Age-adjusted prevalence rates of Crohn's disease (CD) from 1991 to 2006
Sex-specific rates are age-adjusted; total rate is sex- and age-adjusted. The total numbers of CD patients (all Chinese) being followed up in each period are shown. In this instance, prevalence amounts to cumulative incidence

(Table). At diagnosis, 11 (41%) patients presented with mild-moderate disease, whereas eight (30%) had moderate-severe disease and eight (30%) had severe-fulminant disease. During the period reviewed, complications arose in 11 (41%) patients, including lower GI bleeding with shock, intestinal obstruction, intestinal perforation, recto-vaginal fistula, and buttock abscess.

Treatment and outcomes

At the closure date of the study, the median duration of disease in our patient cohort was 81 months (range, 17-200 months). Twenty-three (85%) of the patients took oral 5-aminosalicylates as maintenance treatment, 14 (52%) were taking long-term azathioprine to maintain disease remission and five (19%) were taking steroids. No patient received anti–tumour necrosis factor therapy. During the course of their illness, 16 patients developed clinical relapses, 11 of whom developed at least two relapses. Although most patients were in disease remission (n=23, 85%) at the time of data collection, 13 (48%) had undergone at least one relevant operative procedure for diagnostic purposes or to treat complications during this period. No patient was known to have developed colorectal cancer or died during the period under study, though four were lost to follow-up.

Discussion

Inflammatory bowel disease remains an uncommon disease in Asian regions, and more especially CD. However, its incidence/prevalence has been observed to increase. In a large-scale retrospective study in China, IBD prevalence had increased more than 4-fold from 1990 to 2003.[9] Another local study showed that the annual incidence of CD has increased about 3-fold, from 0.3 per 100 000 in 1986-1989 to 1.0 per 100 000 in 1999-2001,[7] which was higher than the absolute numbers and incidence rates encountered in our study. Nevertheless, both studies noted a rising incidence and prevalence rates. In another study from our centre, the prevalence of ulcerative colitis was also increasing.[23]

Crohn's disease has a predilection to affect young persons. The mean age at diagnosis in our patients was 26 years, most having been diagnosed in the second or third decade of life. Consistent with western[24] and local experience,[7] there appeared to be a bimodal age distribution with a second peak in the fifth decade (Fig 1). In contrast to a western study which showed a slight female predominance,[1] there was a male predominance in our CD patients, which also concurred with other Asian studies.[7,9] Family history and extra-intestinal manifestations were uncommon in Chinese patients[7,9] compared to western cohorts.[25]

Concerning clinical characteristics, the presenting symptoms of Chinese patients were typical of CD. Most presented with abdominal pain and diarrhoea. Disease location was also similar to that noted in other Asian and western studies.[7,9,26,27] Most patients had ileocolonic involvement, followed by Crohn's colitis and ileal disease. However, our patients did not manifest upper GI disease. In contrast to other studies,[7,9,26] most of our patients had non-stricturing and non-penetrating disease.

Crohn's disease seems to be difficult to diagnose; the median duration from symptom onset to diagnosis was 6 months. At diagnosis, a significant proportion of patients had moderate-severe or severe-fulminant disease (30% in each category), five of whom presented as acute emergencies treated by immediate surgical intervention. This state of affairs could be related to delayed diagnoses, owing to lack of disease awareness, by physicians. It is particularly difficult to diagnose small bowel CD, because effective investigative tools are not readily available. Notably, eight (30%) of the patients had operations to confirm the diagnosis (based on histology from surgical specimens). The availability of new diagnostic tools for small bowel disease such as capsule endoscopy and double-balloon endoscopy may facilitate the early diagnosis of CD in the future.[28,29] On the contrary, Asian IBD patients appear to have milder and easier-to-treat disease compared to their western counterparts. In our study, most (85%) of the patients were in disease remission with medical treatment, although 48% underwent surgery at some stage of their illness. The high operative rates were no different from those reported by others.[7,9,26]

A good epidemiological study of IBD should have a well-defined catchment area, up-to-date population data, availability of appropriate diagnostic facilities, uniform criteria for case definition, a common protocol, and an established referral system.[30] Our study fulfilled all these criteria. However, it was hospital-based, which may have under-estimated the true incidence and prevalence of CD and over-estimated disease severity and the risk of IBD complications.[31] Some patients may have consulted private practitioners or herbalists for their disease management. For several reasons we believe that the number of such patients was small in our setting. In Hong Kong, 94% patients requiring health care for chronic diseases attend the public hospital system, due to treatment costs being nominal. Our hospital is situated in a less affluent part of the city, with median household incomes below the overall average in Hong Kong. Residents in our region, therefore rely heavily on the subsidised health care service provided by our hospital. Moreover, there was no private hospital or community gastroenterologist providing expertise in the management of IBD in our catchment area. For these reasons, we had an opportunity to perform a region-based study on the descriptive epidemiology and phenotypes of CD.

Like many other retrospective studies, our study was limited by recruitment bias and discrepancies in our follow-up protocol. Our sample size was small because CD remains uncommon in Hong Kong. Even if one patient chose to be managed in another catchment area, this could significantly influence incidence and prevalence rates. Thus, in view of our small sample size and differences in the background characteristics of our population, our results may not be extrapolated to Chinese populations in other regions.

Conclusions

Growing evidences show that IBD is increasing in Asian regions. Although there are many similarities between Asian and western populations, significant epidemiological and clinical differences exist. Issues such as aetiology, pathogenesis, curative therapy, and colorectal cancer screening strategies for Asian patients remain unanswered. In the future, a well-conducted population-based IBD registry in our own region could help to solve these problems.

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