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A First Study on the Incidence and Prevalence of IBD in Malaysia—Results From the Kinta Valley IBD Epidemiology Study

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Abstract

Background: Inflammatory bowel disease [IBD] is known to be rare in the Asia Pacific region but epidemiological studies are scarce.
Methods: Kinta Valley [Ipoh] was chosen as the sample population. Malaysia has a multiethnic population consisting of Malays, Chinese, and Indians. New cases over 2 years were prospectively captured as well as all known existing cases. Total numbers of the population as a whole and of each ethnic group were obtained. Incidence, prevalence, and mean incidence over two decades were then calculated.
Results: There were 10 new cases of IBD diagnosed from April 2011 to April 2013. The crude incidence rates of IBD, ulcerative colitis [UC], and Crohn's disease[CD], respectively, were 0.68, 0.46, and 0.20 per 100 000 persons. The highest incidence was among the Indians, 1.91 compared with 0.35 and 0.63 per 100 000 persons among the Malays and the Chinese, respectively. The mean incidence of IBD has increased steadily from 0.07 to 0.69 per 100 000 person-years over the past two decades. The UC:CD ratio was 8:1 from 1990 to 2000 and 3.6:1 from 2000 to 2010. The prevalence rates of IBD, UC, and CD, respectively, were 9.24, 6.67, and 2.17 per 100 000 persons. The highest prevalence also was among the Indians: 24.91 compared with 7.00 and 6.90 per 100 000 persons among the Malay and Chinese races, respectively.
Conclusions: The incidence and prevalence rates of IBD are low in Malaysia but the incidence appears to be increasing and marked racial differences exist. As in other Asian countries, the incidence of CD is increasing at a more rapid rate relative to UC.

Keywords: Epidemiology; inflammatory bowel disease; incidence; prevalence; Asia

1. Introduction

Inflammatory bowel disease [IBD] is rare in the Asia Pacific region with the exception of Australia and New Zealand, but epidemiological data from countries such as Japan, Korea, and Hong Kong have shown a clear increase in the incidence and prevalence of this disease which is likely to mirror the rest of the region.[1] However, the true incidence and prevalence in other less developed countries have not been established. Malaysia is part of South East Asia and

like many other diseases in this region, epidemiological studies are scarce due to limitations in resources and other factors. Although nationwide registries such as the National Cancer Registry exist, it is not surprising that IBD, which is considered to be of low disease burden, has not been considered a priority. To date, there have been no data in terms of incidence and prevalence in Malaysia. However, there is a general consensus among the gastroenterologists and other related specialties that the incidence and prevalence of IBD appear to be increasing, in keeping with other Asian countries. In addition to this, data from our own centre have shown that Crohn's disease [CD] runs a similar course as in the West, with a high risk of stricturing and penetrating complications, and surgical rates approaching 50%.[2] Studies from neighbouring Singapore[3] and sub-analysis of our own study have shown young patients are more at risk of aggressive disease. Understanding the epidemiology and clinical aspects of IBD is essential in overcoming the challenges in managing this disease in Malaysia, which has been largely under-recognised and under-treated.

Although there have been previous clinical studies, predominantly from our group at the University of Malaya,[2,4] there has been no true population-based epidemiological study from Malaysia. The Kinta Valley Study represents the first such study from Malaysia and one of few from across the whole of Asia.

The aims of this study were therefore to look at the current incidence and prevalence of IBD, to look at trends in incidence and to examine the socio-demography of the disease in Malaysia.

2. Methods

This study was part of a large collaboration to study the epidemiology of IBD in Asia [ACCESS study], spearheaded by the Chinese University of Hong Kong.[5] The population of Malaysia is 28.5 million and there are three main Asian ethnic groups in Malaysia; Malays, Chinese, and Indians. The sample population chosen was in the geographically defined region of Kinta Valley, approximately 205 km north of Kuala Lumpur.[see Figure 1]. The region consists of the city of Ipoh [643 km^2], the capital of the state of Perak, and its surrounding towns and villages.

Figure 1. Map of Malaysia denoting Ipoh and the capital, Kuala Lumpur.

This area was specifically chosen because it has a stable population with low migration rates to and from other regions in the country.

The population total as well as the ethnic breakdown were obtained from Department of Statistics Malaysia. According to the 2010 census, the population of Kinta Valley is approximately 735 601.[6] The ethnic breakdown in Kinta Valley was as follows: Malays 285 880 [39%]; Chinese 318 546 [43%]; and Indian 104 370 [14%]. The ethnic mix in Kinta Valley is representative of urban populations in Malaysia but not of rural areas where the residents are predominantly Malays.

2.1. Collection of data

Collection of data was painstakingly done. We employed a full-time research assistant who was based in the Kinta Valley throughout the duration of the study. Prior to the commencement of the study, all investigators met for a half-day detailed discussion on the operations of the study. As IBD is a very specialised disease, we endeavoured to capture every case of IBD during the period of the study. Wide publicity through communication with the Malaysian Medical Association of Perak was conveyed to every single practitioner in the Kinta Valley regarding the study. The full-time research assistant periodically [once every 2 weeks] contacted all gastroenterologists, physicians, and surgeons in charge of the study to ensure all cases were prospectively collected. Informed consent was obtained from all subjects.

For the incident cases, all data were initially captured using the standard collection form used in the ACCESS study [which is currently ongoing] and subsequently transferred to an electronic database created for the study. For the prevalence data, we used an existing collection form that has been utilised for many years to capture data from our own patients in the University of Malaya Medical Centre [UMMC].

2.2. Incidence cases

There is only one general hospital in Ipoh, with 990 beds, and three private hospitals that accept gastrointestinal cases. All the registered gastroenterologists and general physicians with a special interest in gastroenterology were identified and contacted as well as surgeons and two pathologists who all have a wide referral pattern throughout the Kinta Valley. There are no registered paediatric gastroenterologists in Kinta Valley and all paediatric gastroenterology cases are referred to adult gastroenterologists. New cases [confirmed Kinta Valley residents] from these hospitals were meticulously captured over a duration of 2 years. Each case was then carefully assessed to ensure that the criteria for the diagnosis of IBD were met based on clinical, endoscopic, histological and radiological features.[7] Infectious enterocolitis including tuberculosis was carefully excluded. Disease location and behaviour were documented according to the Montreal classification.[8]

The crude incidence rates of IBD, ulcerative colitis [UC] and CD were then calculated based on the whole population of Kinta Valley [over 2 years] as the denominator. The incidence rates according to ethnicity were then calculated using the population obtained for each ethnic group. The age-standardised incidence rates were derived using the World Health Organization standard population.

2.3. Prevalence cases

For the prevalence study, all available case notes from each centre, whether active or inactive [ie patients who were lost to follow-up], up till 2013 were carefully examined. All existing cases [confirmed residents] under follow-up by all the hospitals were recruited and attempt was made to contact all resident cases who were lost to follow-up. Again, each case was carefully reviewed to confirm the diagnosis of IBD.

The prevalence was then again calculated based on the whole population and the population of each ethnic group.

2.4. Calculation of incidence trend

The incidence trend was calculated using retrospective data. For the numerator, we documented the year of diagnosis for all confirmed cases of IBD obtained from all the available case notes in each of the four hospitals, regardless of whether or not the patient was under follow-up. For the denominator, we estimated the population of Kinta Valley for each year from 1990 till 2010. Population data for the years 1990, 2000, and 2010 were obtained from the Department of Statistics. We then used the published population growth rate of 1.39% from 1990 to 2000 and 1.68% from 2000 to 2010 to estimate the population for all the years in between [see Table 1].

Subsequently, we grouped the cases diagnosed over 5-year periods [1990–1994, 1995-1999, 2000-2004, 2005–2009] as the numerator and the sum of the population over the same 5 years was used as the denominator. Mean crude incidence was then calculated and expressed as number of cases per 100 000 person-years. The details of the calculation are summarised in Table 1.

2.5. Baseline demography and disease phenotype

All cases [new and existing] were carefully evaluated. Baseline demography and disease characteristics were recorded.

3. Results

3.1. Incidence of IBD in Malaysia

Ten new cases of IBD, diagnosed from April 2011 to April 2013, were recruited: 7 UC and 3 CD. The baseline demography was as follows: median age 32.5 [range 13–65] years; male:female ratio 7:3;

Malays 2 cases, Chinese 4, Indians 4. Among the cases of patients with UC, 4 were left-sided colitis [E2], 3 were proctitis [E1]. Among the CD patients, disease locations were as follows: ileocolon [L3] 2, colon [L2] 1. All three CD patients had non-penetrating non-stricturing disease.

The crude incidence rates of IBD, UC, and CD, respectively, were 0.68 (95% confidence interval [CI] 0.55–0.81), 0.46 [95% CI 0.44–0.51] and 0.20 [95% CI 1.81–2.27] per 100 000 persons, [Figure 2]. The age-standardised incidence rates of IBD, UC, and CD were 0.67, 0.49, and 0.18 per 100 000 persons, respectively. The highest incidence was among the Indians, 1.91 [95% CI 1.73–2.10] per 100 000 persons, compared with 0.35 [95% CI 0.30–0.40] and 0.63 [95% CI 0.57–0.69] per 100 000 persons among the Malays and the Chinese, respectively [Figure 3].

3.2. Incidence trend

The crude mean incidence rates of IBD, UC, and CD over the past two decades are shown in Table 1. The incidence of IBD has steadily increased over the past two decades; from 0.07 per 100 000 population-years in 1990-1995 to 0.69 per 100 000 population-years in 2005–2010. Compared with the previous decade, there was a marked increase in the incidence of CD relative to UC; the UC:CD ratio was 8:1 from 1990–2000 but this had decreased to 3.6:1 from 2000 to 2010. [Figure 4].

3.3. Prevalence of IBD

A total of 76 case notes of all known patients diagnosed with IBD in each centre were reviewed, whether active or inactive [ie patients who were lost to follow-up]. Six patients were not contactable. A total of 68 confirmed resident cases of IBD was identified, among whom 66 were still under regular follow-up in any of the hospitals

Table 1. Calculation for incidence trend in inflammatory bowel disease [IBD].

| Year	Ulcerative colitis [UC]	Crohn's disease [CD]	IBD-unclassified	Population	Cumulative population[a]	IBD N, mean incidence[b]	UC N, mean incidence[b]	CD N, mean incidence[b]	IBD unclassified N, mean incidence[b]
1990	0	0	0	549198	2 823 395	2	2	0	0
1991	0	0	0	556832		0.07	0.07	0	0
1992	1	0	0	564571					
1993	0	0	0	572419					
1994	1	0	0	580375					
1995	0	0	0	588443	3 024 431	8	6	1	1
1996	1	0	0	596622		0.26	0.20	0.03	0.03
1997	2	1	0	604195					
1998	1	0	1	613323					
1999	2	0	0	621848					
2000	1	0	0	622106	3 216 812	10	9	0	1
2001	3	0	0	632557		0.31	0.28	0	0.03
2002	1	0	1	643184					
2003	3	0	0	653989					
2004	1	0	0	664976					
2005	5	1	0	676148	3 496 257	24	16	7	1
2006	1	0	0	687507		0.69	0.46	0.20	0.03
2007	4	2	0	699057					
2008	4	1	1	710802					
2009	2	3	0	722743					

The first three columns denote the cases of UC, CD and IBD unclassified for each given year. The population figures for 1990, 2000, and 2010 were obtained from Department of Statistics, Malaysia. The intermediate years were estimated using a population growth rate per year of 1.39% from 1990 to 2000 and 1.68% from 2000 to 2010.

[a]Denotes the sum of the population over 5 years.

[b]Per 100 000 person-years.
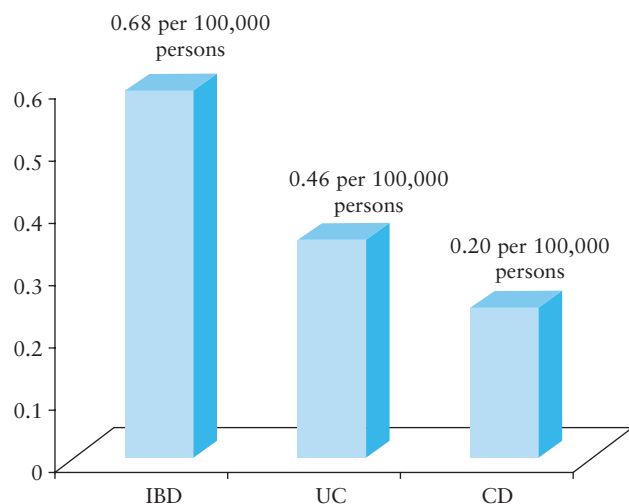
Figure 2. Incidence of inflammatory bowel disease [IBD], ulcerative colitis [UC], and Crohn's disease [CD] in Malaysia.
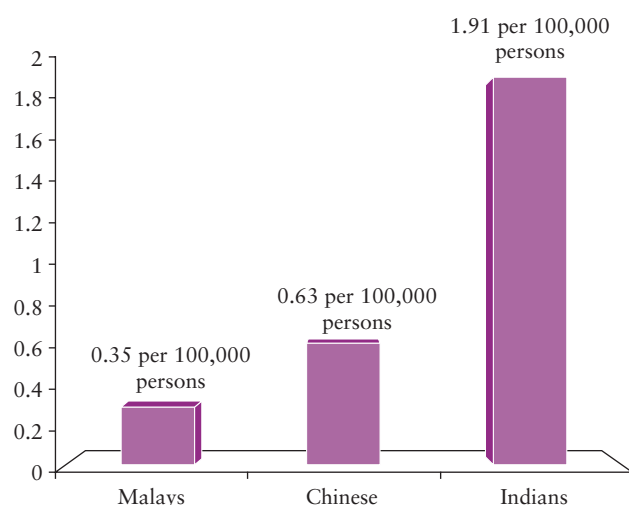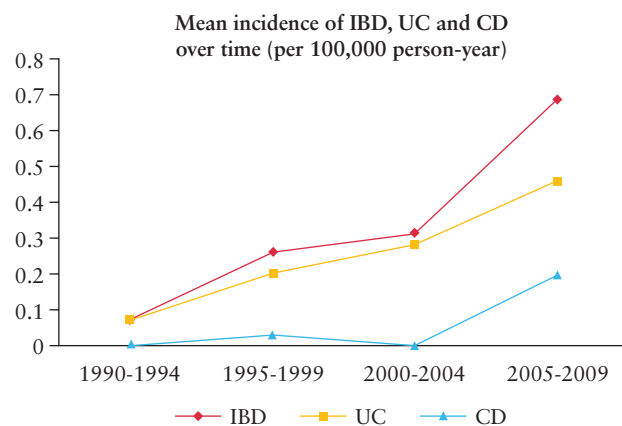

Figure 3. Incidence of inflammatory bowel disease [IBD] according to ethnic group.

Figure 4. Incidence trend of inflammatory bowel disease [IBD], ulcerative colitis [UC], and Crohn's disease [CD] in Malaysia over two decades.
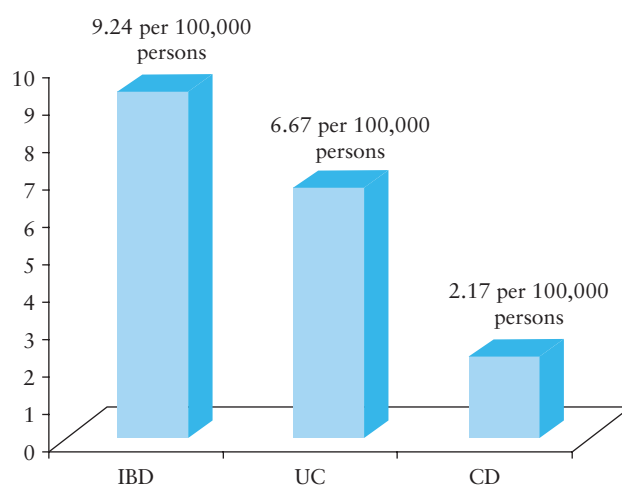
Figure 5. Prevalence of inflammatory bowel disease [IBD], ulcerative colitis [UC], and Crohn's disease [CD]IBD in Malaysia.
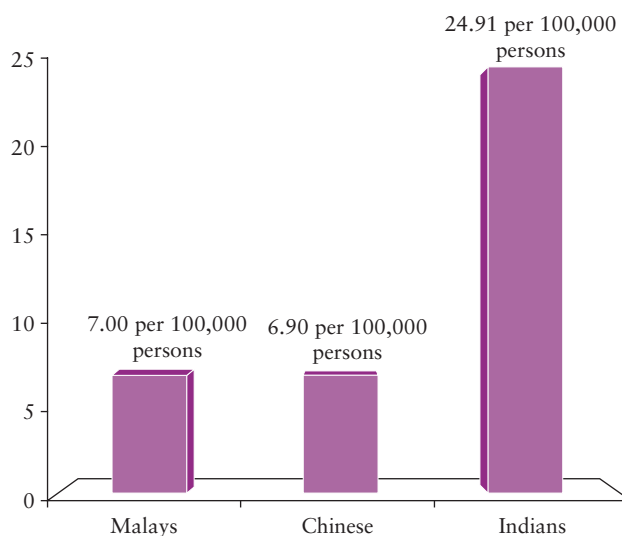
Figure 6. Prevalence of inflammatory bowel disease [IBD], ulcerative colitis [UC], and Crohn's disease [CD]IBD according to ethnic group.

[some had switched from a private hospital to the government hospital due to financial constraints] and two not under regular follow-up. The distribution of the cases was as follows: UC 49 [72.1%], CD 17 [25%], and IBD unclassified 2 [2.9%]. The prevalence rates of IBD, UC, CD, and IBD unclassified, respectively, were 9.24 [95% CI 7.10–11.40], 6.67 [95% CI 4.80–8.53], 2.17 [95% CI 1.11–3.24], and 0.41 [95% CI 0.32–0.50] per 100 000 persons [Figure 5]. The highest prevalence was again among the Indians: 24.91 [95% CI 15.30–35.50] per 100 000 persons as compared with 7.00 [95% CI 3.93–10.10] and 6.90 [95% CI 4.02–9.79] per 100 000 persons among the Malay and Chinese races, respectively [Figure 6].

The demography and clinical characteristics of the cases are presented in Table 2.

4. Discussion

This is the first detailed epidemiological study of its kind on IBD from Malaysia. The study was conducted with great attention to detail and although it was hospital and clinic based, we are confident

Table 2. Demography and clinical characteristics of inflammatory bowel disease [IBD] prevalent cases.

Characteristics	Ulcerative colitis [and IBD unclassified]	Crohn's disease
Number	51	17
Median age in years	45	28
Gender		
Male	22 [43.1%]	12 [70.6%]
Female	29 [56.9%]	5 [29.4%]
Ethnicity		
Malays	15 [29.4%]	5 [29.4%]
Chinese	17 [33.3%]	5 [29.4%]
Indians	19 [37.3%]	7 [41.2%]
Family history	0 [0%]	1 [5.9%]
Smoking	0 [0%]	3 [17.6%]
Duration of disease [years]	7	5
Disease extent		
Proctitis [E1]	15 [29.4%]	N/A
Left sided [E2]	17 [33.3%]	N/A
Extensive [E3]	19 [37.3%]	N/A
Disease location		
Ileal [L1]	N/A	5 [29.4%]
Ileal and upper disease [L1 + L4]		1 [5.9%]
Colon [L2]	N/A	8 [47.1%]
Ileocolon [L3]	N/A	3 [17.6%]
Isolated upper disease [L4]	N/A	0 [0%]
Disease behaviour		
Non-penetrating non- stricturing [B1]	N/A	10 [58.8%],
Stricturing [B2]	N/A	5 [29.4%]
Penetrating [B3]	N/A	2 [11.8%].
Perianal [p]	N/A	3 [17.6%]
Complications		
Extra-intestinal	11[21.6%]	4 [23.5%]
Colorectal carcinoma	0 [0%]	0 [0%]
Small bowel carcinoma	0 [0%]	0 [0%]
Acute severe colitis	0 [0%]	0 [0%]
Surgery	0 [%]	4 [23.5%]
Treatment[a]		
5-aminosalicylates	50 [98%]	12 [70.6%]
Thiopurines	14 [27.5%]	10 [58.8%]
Methotrexate	0 [0%]	1 [5.9%]
Anti-tumour necrosis factor	1 [2%]	2 [11.8%]
Corticosteroids	37 [72.2%]	17 [100%]

N/A, not applicable.

[a]Ever exposed.

that we have captured the majority if not all the incident patients with IBD during the study. This study is an extension of the ACCESS study, which is a pan-Asian Pacific incidence study whose findings have now been published.[5] Prior to the ACCESS study, there were minimal data on the epidemiology of IBD in the Asia-Pacific region but, for the first time, we now have the age-standardised incidence rates in most of the countries This study confirms that there is a wide variation in the incidence of IBD in Asia, ranging from 0.54 to 3.44 per 100 000 population-years. However, in addition to the incidence, we sought to also establish the prevalence of the disease as well as the trend in incidence, as other studies from Japan, Korea, and Hong Kong have shown a clear increase in incidence over the past few decades.[9,10,11]

From our study it appears that the incidence of IBD is indeed low in our population, with a rate of about 0.68 per 100 000 population per year, and this is in sharp contrast to the incidence rates in Australia and New Zealand of 23.7 and 25.2 per 100 000 population-years,

respectively.[5,12] The prevalence is also low in our population, at 9.24 per 100 000. As the population of Malaysia is approximately 28.5 million, one could estimate that there are approximately 2000 to 3000 cases of IBD in Malaysia.

We also calculated, albeit retrospectively, the time trends of incidence of the disease from available records. When looking at the incidence trend, it appears that there is an increasing incidence in Malaysia over the past two decades. When analysed further, it is clear that the main reason is the sharp increase in the rise of CD.

This change in demographics is consistent with that seen worldwide; in most countries, the incidence of UC is significantly higher than CD but the gap becomes narrower over time[13] and, in some countries such as New Zealand and Australia, the incidence of CD even exceeds that of UC.[5,12] The reason for this observation is not entirely clear but is probably due to both an increase in the diagnosis of CD and a true increase in the incidence of CD compared with UC.

If CD is indeed increasing, then the answer must lie in as yet unidentified alterations in the environment.

Another main finding from this study is the clear difference in incidence and prevalence of this disease among the three major ethnic groups, in that the disease appears to be predominant among Indians. This finding has previously been reported from our hospital-based studies[2,14] and also from studies in neighbouring Singapore.[15] When compared with other Asian countries, the incidence and prevalence of IBD appear to be much higher in India, with an incidence and prevalence similar to Western populations.[16] Furthermore, specific IBD mutations identified in our population are higher among the Indian ethnic group.[17]

Although not the main aim of this study, we also looked at the clinical characteristics of patients with UC and CD. The findings are similar to our previously published studies on UC[4] and CD[2] in that risk factors such as smoking and family history are uncommon in our population. There were no documented cases of colorectal carcinoma. In terms of clinical course, our previous study confirmed a high risk of stricturing and penetrating complications in our CD population with correspondingly high rates of surgery. In this cohort, a fifth of patients had undergone surgery, which is a high percentage considering that the median duration of disease was 5 years. However, it must be pointed out that the total number of cases in this study was small which means that descriptive analysis of the disease may not be reflective of the true clinical phenotype and course of IBD in Malaysia.

The main strength of this study is that we have defined a well-circumscribed geographical area. We have judiciously contacted all the main doctors involved in diagnosing and managing the cases and have prospectively collected all incident cases from all the hospitals in the catchment area over a period of 2 years. All incident cases as well as existing cases for the prevalence study were carefully evaluated to ensure that the clinical, endoscopic and radiological findings were consistent with IBD. We are confident that almost all cases were captured as IBD, unlike functional cases, are usually referred to hospitals and not managed by primary care physicians. This is because unlike in the West, IBD is still an uncommon disease and most primary physicians are not comfortable in managing the condition. However, we could not completely rule out the fact that mild cases of proctitis may have been treated at a primary care level and therefore not captured in our data. It is also possible that a few patients chose to be evaluated and followed up in the capital city, Kuala Lumpur, and were also consequently not captured. It is also important to point out that whereas we feel the study is representative of an urban population in Malaysia, the incidence and prevalence may not be representative of the whole country where there are still large rural areas. Given that these areas are mostly made up of either ethnic Malays and other indigenous populations who are less predisposed to developing IBD, the true incidence and prevalence may be actually lower than calculated. In addition to this, urbanisation itself is thought to be a significant predisposing factor in the development of IBD. An interesting study would be a comparative one between the rural and urban Malaysian populations.

Our major limitation is our secondary aim of looking at the incidence trend. As we did not have data from a longitudinal prospective study, we went back to analyse all the records and computed the incidence trend based on the year of diagnosis and the estimated population during the same time period. Although all the available records, whether active or inactive, were carefully analysed, it is expected that there will be missed cases due to the fact that the data were collected retrospectively.

In conclusion, we present for the first time the incidence and prevalence of IBD in a multi-ethnic East-Asian population. The study has shown that although the incidence and prevalence rates of IBD are low in Malaysia, the incidence appears to be increasing as in other Asian countries. The incidence of CD is increasing at a more rapid rate relative to UC. This study confirms previous observations that the disease is predominantly seen in Indians.

Conflict of interest statement

None.

Acknowledgement

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