The Incidence and Prevalence of Inflammatory Bowel Disease in the Jewish and Arab Populations of Israel*

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ABSTRACT:
Background: Temporal trends in the incidence of inflammatory bowel disease (IBD) in the Arab and Jewish populations in Israel have been poorly described.
Objectives: To compare the annual incidence and prevalence rates of Crohn's disease (CD) and ulcerative colitis (UC) in the Arab and Jewish populations in Israel between the years 2003 and 2008.
Methods: We applied a common case identification algorithm to the Clalit Health Services database to both determine trends in age-adjusted incidence and prevalence rates for IBD in both populations during this period and estimate the burden of IBD in Israel.
Results: The incidence of CD in the Arab population increased from 3.1/100,000 in 2003 to 10.6/100,000 person-years in 2008, compared with a decrease in the Jewish population from 14.3/100,000 to 11.7/100,000 person-years for the same period. The incidence of UC in the Arab population increased from 4.1/100,000 in 2003 to 5.0/100,000 person-years in 2008, a low but stable rate, compared with a decrease from 16.4/100,000 to 9.5/100,000 person-years for the same time period in the Jewish population. The prevalence of both diseases increased due to the accumulation of incident cases but remained much lower among Arabs.
Conclusions: Understanding the factors underlying the differences in incidence and prevalence of IBD in the Jewish and Arab populations may shed light on the genetic and environmental factors associated with these diseases.

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KEY WORDS: inflammatory bowel disease (IBD), Crohn's disease (CD), ulcerative colitis (UC)

Inflammatory bowel disease (IBD) is a chronic disease affecting the gastrointestinal tract. The two main forms of IBD are Crohn's disease (CD) and ulcerative colitis (UC). Although the precise etiology of IBD is unknown, its development is likely to be related to a maladaptive immune response to environmental and microbial triggers among genetically susceptible individuals. Accurate epidemiological studies of IBD are important for appreciating the impact on public health and for planning appropriate health services [1-3]. In this context, population-based studies that capture all health system contacts and reflect the true burden of disease provide the best basis for decision making. Moreover, epidemiological studies could offer clues to the etiology of these diseases. A number of population-based studies from Europe and North America have identified trends in disease prevalence that have regional implications but may not be broadly applicable for planning in other countries [4,5].

Little is known about the epidemiology of ethnic differences in the occurrence of IBD in Israel. In our previous studies of Diaspora and Israeli Jews, including populations of communal settlements (kibbutzim) [6-9], we found an increase in IBD prevalence with time among Ashkenazi, Sephardic and Israeli-born Jews. Our previous study of the Israeli Arab population conducted on a small cohort [10], and other studies from localized geographical areas such as the upper Galilee [11] and the Negev region [12], showed a low prevalence rate of IBD.

The aim of the present study was to identify the annual prevalence and incidence rates of IBD in Israel for the 6 years prior to 31 August 2008, and to identify temporal trends in Jewish and Arab populations in Israel.

PATIENTS AND METHODS

CLALIT HEALTH SERVICES DATABASE

Clalit Health Services is the largest health service provider in Israel, providing healthcare to 53.31% of the Israeli population. The organization maintains a central database for all its members for administrative purposes. Data for this study were obtained from the Business Objects database (BOBJ, SAP, Germany) belonging to Clalit Health Services. This database contains individual-level healthcare entries for more than 70 million customer interactions per year, including physician office visits, outpatient visits, hospital admissions, nurse practitioner encounters, laboratory and radiology services, pharmacy data, and billing. We searched for diagnoses of CD or UC between the years 2003 and 2008 based on International Classification of Diseases, 9th revision, diagnosis code of 555.xx (CD) and 556.xx (UC) during the capture period. Individuals

with one or two health service contacts for possible IBD were excluded to enhance the specificity. Demographic data including age, gender and ethnicity were extracted from the central database for each of the identified individuals.

New cases of IBD for each year of the study were obtained from the Clalit Health Services database to calculate incidence; similarly, all cases of IBD were used to calculate the prevalence rates. Population data were extracted both from the Clalit Health Services database and the Israel Central Bureau of Statistics Census for 2008 [13].

The study was approved by the Rabin Medical Center Ethics Committee according to the Helsinki Declaration and registered with the National Institutes of Health, USA.

ANALYSES

The characteristics of the participants are presented as arithmetic mean (± SD). We calculated the incidence rate of CD and UC for the years 2003 to 2008 from newly identified cases. We calculated the point prevalence of CD and UC as the number of cases per 100,000 enrollees for a specific year (measured on 31 August). Differences between incidence rates were compared by calculating incidence rate ratios. Differences in prevalence were compared using the chi-square test. All tests were two-sided, and the results were considered significant at a P value of < 0.05. Analyses were performed with IBM SPSS Statistics 20 software (IBM Inc., Chicago, IL, USA).

RESULTS

The total number of enrollees in Clalit Health Services was 3,727,928 in 2003 and 3,904,781 in 2008. After excluding 1787 individuals in whom the diagnosis of IBD was not adequately established, there were 7122 cases in 2003 with a prevalence of 191/100,000, and 12,378 cases in 2008 with a prevalence of 317/100,000.

CROHN'S DISEASE

There were 3261 prevalent cases of CD in 2003. Of 6062 prevalent cases in 2008, 51.3% were male [Table 1].

- **Incidence**

The incidence of CD in the population studied was 11.6/100,000 in 2003 and 11.4/100,000 person-years in 2008, indicating an unchanged rate [Table 2]. However, in the Arab population, rates increased from 3.1/100,000 in 2003 to 10.6/100,000 compared with a decrease from 14.3/100,000 to 11.7/100,000 for the same period in the Jewish population ($P < 0.0001$) [Table 2]. The peak incidence occurred between age 25 and 35 in both populations.

- **Prevalence**

The prevalence of CD in the total Israeli population was 87.6/100,000 in 2003 and 139.2/100,000 persons in 2008 [Table 3].

Table 1. Characteristics of Israeli patients with inflammatory bowel disease (IBD) in 2008

Parameter	CD			UC		
	Total	Jews	Arabs	Total	Jews	Arabs
Total	7005	6237	768	7163	6532	631
Excluded	943	802	141	844	726	118
Included	6062	5435	627	6319	5806	513
Female	2955 (48.7%)	2690 (49.5%)	265 (42.3%)	3234 (51.2%)	3011 (51.9%)	223 (43.5%)
Males	3106 (51.3%)	2744 (50.5%)	362 (57.7%)	3085 (48.8%)	2795 (48.1%)	290 (56.5%)
Age (years) at time of survey (mean ± SD)	45.0 ± 12.5	46.3 ± 20.7	29.8 ± 22.3	57.0 ± 14.7	56.6 ± 19.6	45.9 ± 18.3
Colonoscopies performed	4909	4081	828	4943	4072	871
Sigmoidoscopies performed	2094	1334	760	2259	1734	525

Table 2. Annual incidence rates for Crohn's disease (CD) and ulcerative colitis (UC) between 2003 and 2008

Year	CD			UC		
	Total Israeli population	Jews	Arabs	Total Israeli population	Jews	Arabs
2003	11.6	14.3	3.1	13.4	16.4	4.1
2004	13.7	16.4	5.2	14.3	17.1	5.5
2005	11.3	13.8	4.0	11.3	13.3	5.3
2006	13.3	14.5	9.8	10.6	12.7	4.3
2007	13.1	14.6	8.5	10.4	12.4	4.4
2008	11.4	11.7	10.6	8.3	9.5	5.0

Table 3. Annual prevalence rates for Crohn's disease (CD) and ulcerative colitis (UC) between 2003 and 2008

Year	CD			UC		
	Total Israeli population	Jews	Arabs	Total Israeli population	Jews	Arabs
2003	87.6	108.0	22.6	103.5	127.8	27.1
2004	100.5	124.1	27.0	117.8	145.7	31.6
2005	111.3	138.0	30.0	128.6	159.1	36.1
2006	122.1	151.3	34.2	137.9	170.7	40.4
2007	134.6	164.6	45.6	146.6	181.5	43.5
2008	139.2	177.0	55.9	155.4	192.3	47.8

Differences in prevalence were found between ethnic groups in Israel. The prevalence rates increased from 108.0/100,000 in 2003 to 177.0/100,000 in 2008 among Jewish Israelis, and from 22.6/100,000 to 55.9/100,000 among Arab Israelis during the same period [Table 3]. Among Jewish Israelis, 50.5% of subjects with CD were male, compared to 57.7% among Arab Israelis (not significant) [Table 1].

ULCERATIVE COLITIS

In the total Israeli population, there were 3861 cases of UC in 2003, and of the 6319 cases in 2008, 48.3% were male [Table 1].

- **Incidence**

The incidence for UC in the studied population was 13.4/100,000 in 2003 and 8.3/100,000 person-years in 2008, indicating a decrease during the period studied. However, in the Arab population, incidence increased from 4.1/100,000 in 2003 to 5.0/100,000 in 2008, compared with a decrease from 16.4/100,000 to 9.5/100,000 for the same years in the Jewish population [Table 2]. The peak incidence occurred between age 25 and 35 in both populations.

- **Prevalence**

The prevalence rate of UC was 103.5/100,000 in 2003 and 155.4/100,000 persons in 2008 [Table 3]. Major differences in prevalence were found between ethnic groups in Israel. The prevalence rates increased from 127.8/100,000 in 2003 to 192.3/100,000 in 2008 for the Jewish population [Table 3] compared with 27.1/100,000 to 47.8/100,000 in the Arab population for the same time period.

DISCUSSION

In 1995 the introduction of a new government law made it compulsory for all Israeli individuals to receive healthcare from one of four Health Services. Since 1999/2000 it has been mandatory for the Clalit Health Services to register all chronic diseases in a computerized database. We were able to use this database to obtain statistics to identify the incidence and prevalence rates of IBD in Israel. We found that the incidence of CD was unchanged in the Israeli population between the years 2003 and 2008. However, when the data were analyzed according to ethnicity there were significant differences between the Arab and Jewish populations. The incidence of CD among Arabs was low in 2003 but increased more than threefold during the study period, compared with a decrease in CD incidence in the Jewish population. Therefore, incidence data that are not stratified for ethnicity may be erroneously interpreted as stable during the period studied, whereas in reality we saw a significant increase among Arab Israelis and a significant decrease among Jewish Israelis. By 2008 the incidence of CD in Arabs was similar to that of the Jews.

The incidence for UC declined in the total population with a more marked decline among Jews, and a slight increase among Arabs. The dramatic increase in CD is underscored by the fact that the incidence of UC and CD was similar in 2003, but in 2008 the incidence of CD was double that of UC. The prevalence rate in the total population for UC was higher than CD both at the beginning and at the end of the study period, but the difference narrowed by the end date. In summary, there was a dramatic increase in the incidence of CD in the Arab population, and a significant decline in the incidence of UC among Jews.

Since the first publication on the epidemiology of IBD in Israel [11,12,14,15] several other studies have been conducted in regional geographic sites, in hospitals, on kibbutzim, and in the Israeli Arab population [6-10]. To date no study has been conducted to compare epidemiological trends in the Jewish and Arab populations in Israel. In a study of UC in northern Israel from 1965 to 1994, the mean annual incidence rate of UC was 3.5/100,000 person-years. Prevalence rates for UC were 87/100,000 in the Jewish, and 27/100,000 persons in the Arab populations [11]. In a study of 61,299 Bedouin Arabs living in southern Israel, 8 patients with IBD were diagnosed between 1981 and 1990. The prevalence rates were 9.8/100,0000 and 3.2/100,000 for UC and CD, respectively [12]. In a previous population-based survey in 2008 we found a prevalence rate of 32/100,000 for CD and 22/100,000 for UC in the Israeli Arab population. However, case findings may have been a limitation in that study [10].

There is a paucity of studies describing the epidemiology of IBD in Arab populations. The incidence of UC in Kuwait in 2003 was 2.8/100,000 person-years [16]. In Lebanon the prevalence rate of UC was 106.2/100,000 persons and the incidence 4.1/100,000 person-years [17]. In central Saudi Arabia, the incidence and prevalence rates of IBD in the pediatric population were 0.5/100,000 person-years and 5/100,000 persons, respectively [18]. In Libya, the prevalence of IBD in childhood was 3.6/100,000 persons and the incidence IBD 0.9/100,000 person-years [19].

The incidence and prevalence of IBD in the Israeli Arab population appears to be considerably higher than in the Arab population in neighboring Arab countries. Reasons for this difference may include dissimilarity in the structure of the health services, case identification and registration, and follow-up. However, we cannot exclude the possibility that an interplay between environmental factors, microbial factors, and genetic shifts may account for the increase and decrease in IBD incidence in Arab and Jewish populations, respectively, over the study period. Various environmental factors have been associated with the development of IBD, such as socio-economic factors, western lifestyle, exposure to smoking and pollution, diet, mode of birth, and early exposure to antibiotics [20]. Early-childhood infectious diseases, including gastroenteritis and respiratory infections, appear to be protective [21]. Although we did not have the capacity to assess these factors in the present study, it is unlikely that the changes we observed are accountable to a single factor alone. Rather, it is likely that the increase in IBD incidence among Arab Israelis is due to the gradual urbanization of their communities. This phenomenon has been well-described in Europe occurring at the time of the industrial revolution, and more recently in China in parallel

with the modernization of society [22]. However, we are not aware of reports of the reverse occurring, where a decrease in IBD incidence is observed in a high-risk population immigrating to a low-risk geographical area, which we observed in our Jewish Israeli cohort – a group comprising many who had immigrated from Europe to the Middle East.

Epigenetic factors are likely to be responsible for mediating the interaction between environmental stimuli and the host genome. Over 160 susceptibility loci have been identified for IBD, the vast majority shared by both CD and UC. These include genes such as *NOD2*, *PTPN22*, *CARD9*, *IL1R2*, *REL*, *SMAD3*, and *PRDM1*, which confer defects in the function of key components of the innate and acquired immune system such as *IL23R*, *IL12B*, *JAK2*, and *STAT3* [23]. It is unknown what degree of overlap exists in genetic and epigenetic factors between Arab and Jewish Israelis with IBD, and whether this changed over the study period.

This present study has several strengths. The population from which data were extracted comprises more than 50% of the total Israeli populace and is representative of the entire population. In addition, case identification has been shown to be accurate and identical for Arabs and Jews, as both populations receive medical services within the same organization. Limitations of the study include problems of case identification from a database not designed specifically to rigorously define and encapsulate all cases of IBD.

CONCLUSIONS

We found diverging trends in the epidemiology of IBD in the Arab and Jewish populations of Israel. The most dramatic change was the steep rise in the incidence of CD among Israeli Arabs. Further studies are needed to identify the genetic and environmental factors that may account for these changes.

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"Common sense is not so common"

Voltaire (1694–1778), French Enlightenment writer, historian and philosopher famous for his wit, his criticism of Christianity, especially the Roman Catholic Church, and his advocacy of freedom of religion, freedom of speech, and separation of church and state

"One man's ways may be as good as another's, but we all like our own best"

Jane Austen (1775–1817), English novelist known primarily for her six major novels, which interpret, critique and comment upon the British landed gentry at the end of the 18th century