



## Trends in Inflammatory Bowel Disease- Comparison Between the Arab and Jewish Population in Israel

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### Abstract

**Introduction:** Genetic and environmental factors have a major influence on the pathophysiology of inflammatory bowel disease (IBD). Older studies reported a very low prevalence of IBD among the Arab population in Israel.

**Objective:** Evaluate the current prevalence and disease characteristics of IBD in the Israeli-Arab population and to compare them to the Jewish population in the same area.

**Methods:** Electronic medical records of all patients insured in the Sharon-Shomron district of Clalit Health Services were reviewed until December 2012. Files of all adults (> 18 years) with a diagnosis of IBD were retrieved.

**Results:** 616,338 patients were insured in the district - 185,510 Arabs and 430,828 Jews. 2050 Jewish and 263 Arab patients met the criteria for IBD (prevalence of 0.48% and 0.14% respectively,  $p < 0.001$ ). Arab patients were younger at diagnosis ( $35.6 \pm 16.2$  vs.  $41 \pm 18.8$  y,  $p < 0.001$ ), had more exacerbations (58.6% vs. 39.5%), anemia (52.1% vs. 39.5%), hypoalbuminemia (33.5% vs. 25.7%) and hypocholesterolemia (53.6% vs. 44%) (all  $p < 0.01$ ). The Arab patients received more oral steroids (46% vs. 36%,  $p < 0.01$ ). More Jewish patients underwent colonoscopy and bone densitometry (43% vs. 32% and 20% vs. 12%, respectively,  $p < 0.01$ ). Arab patients had more IBD-related hospitalizations (37% vs. 28%,  $p < 0.01$ ), but had the same rate of IBD-related surgery compared to the Jewish patients.

**Conclusions:** Prevalence of IBD among the Israeli-Arab population is increasing, but remains lower than among the Jewish population. Arab patients are younger and have more active disease. Our findings support the central role of genetic and environmental factors in the phenotypic expression of IBD, while underscoring ethnic and cultural differences.

### Keywords

Ethnicity, Jews, Arabs, Israel, Compliance, Prevalence, Comparison

important factors in the pathophysiology of the disease. Ashkenazi-Jewish ancestry is considered a major risk factor for the development of IBD [6]. However, more recent studies have demonstrated an increasing incidence of IBD among the Sephardic-Jewish population [1] as well as among non-Jewish ethnic groups [7]. Information about IBD in Arab populations is scarce [8]. In Israel, older studies reported very low to no incidence of IBD among the Arab population [9-11], and a more recent study [12], although small, confirmed the low prevalence. Westernization and increased sanitation are considered some of the reasons for the increasing incidence of IBD among certain populations [13]. Over time, improvements in quality of life measured by life expectancy, infant mortality, infections, average household size and education have been noted in the Israeli-Arab population [14,15]. We evaluated the current prevalence and characteristics of IBD among the local Arab and Jewish population to gain further insight into the pathophysiological factors noted above.

### Methods

Clalit Health Services is the largest health maintenance organization in Israel, and insures more than 600,000 people in the Sharon- Shomron district. The area is significant for two distinct homogenous ethnic populations (Arab and Jewish). Electronic medical records of all patients insured in this health district were reviewed. The files of adults (> 18 years) with a diagnosis of IBD (ulcerative colitis, proctitis, Crohn's disease) were retrieved. Age at diagnosis, gender, ethnicity, type of IBD (UC/CD), duration of disease, disease activity, IBD related hospitalizations and surgery, IBD related medical treatment, laboratory results, co-morbidities and non-IBD medical treatment were reviewed. The diagnosis of IBD was established when confirmed by a gastroenterologist and when acquisition of IBD related drugs was documented by the pharmacy, for at least 3 months. Disease exacerbation was diagnosed when both CRP and platelet counts were elevated (CRP > 1 mg/dl, platelets > 450,000 k/ $\mu$ l). Anemia was defined as a hemoglobin level  $\leq 12$  mg/dl in men and  $\leq 11$  mg/dl in women. Hypoalbuminemia was defined as less than 3.5 mg/dl and hypocholesterolemia as less than 140mg/dl.

Data were analyzed using Microsoft Excel software and SPSS version 20 (Statistical Package for the Social Sciences, SPSS Inc.,

### Introduction

The prevalence of IBD in Israel [1], and in the rest of the world [2,3] is increasing. Genetics [4] and the environment [5] are both

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**Table 1:** Characteristics and demographics of the study populations.

	Jewish	Arabs	p
Total population	431,828 (70.1%)	184,510 (29.9%)	
IBD patients	2,050	263	
Prevalence	480/100.000	140/100.000	< 0.001
Age at diagnosis (y)	41.1 ± 18.8	35.6 ± 16.2	< 0.001
BMI	25.3 ± 6	25 ± 5.1	0.64
Male/Female	994 (48.5%)/1056 (51.5%)	131 (49.8%)/132 (50.2%)	0.68
CD/UC	1,070 (52%)/980 (48%)	134 (51%)/129 (49%)	0.7
Diabetes	224 (10.9%)	47 (17.9%)	< 0.001
Dyslipidemia	789 (38.5%)	73 (27.8%)	< 0.001
Lipid lowering drugs	338 (16.5%)	23 (8.7%)	< 0.001
NSAID's use	591 (25.1%)	81 (30.8%)	0.5
Aspirin use	550 (26.8%)	66 (25.1%)	0.54

CD: Crohn's Disease, UC: Ulcerative Colitis, NSAIDS: Non-Steroidal Anti-Inflammatory Drugs.

**Table 2:** Laboratory and imaging data.

Test data	Jewish	Arabs	p
Anemia(g%)	809 (39.5%)	137 (52.1%)	< 0.001
Hypoalbuminemia(mg/dl)	257 (25.7%)	88 (33.5%)	< 0.001
Hypocholesterolemia(mg/dl)	901 (44%)	141 (53.6%)	< 0.001
Exacerbations	979 (47.8%)	154 (58.6%)	< 0.001
Colonoscopies	889 (43.2%)	85 (32.3%)	< 0.001
Bone density spectrometry	423 (20.6%)	32 (12.2%)	< 0.001
Small bowel imaging	499 (24.3%)	69 (26.2%)	0.54
Hospitalizations	575 (28%)	99 (37.6%)	< 0.001
Surgery	194 (9.5%)	20 (7.6%)	0.32

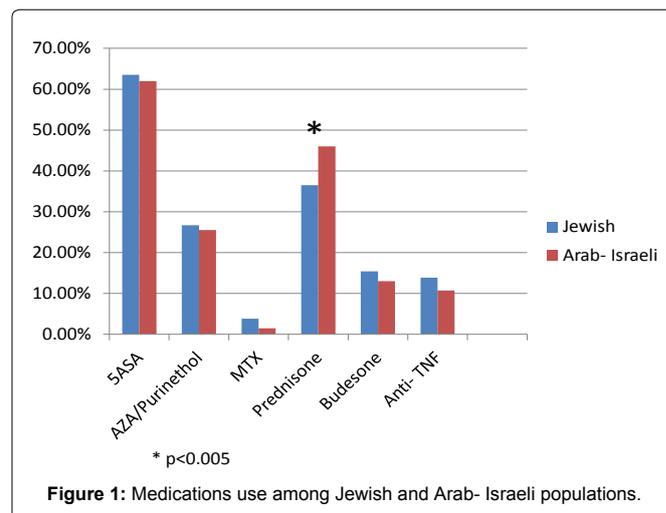
Chicago, USA. Student's t-test, and the  $\chi^2$  test, was used. Data are shown as mean ± standard deviation (SD). A P value < 0.05 was considered statistically significant.

## Results

A total of 616,338 patients were registered as insured by Clalit Health Services in the district until December 2012. Of these, 184,510 (29.9%) belonged to the Arab population and the rest were Jewish (Table 1). Altogether, 2,050 Jewish and 263 Arab patients met the criteria for IBD in adults (prevalence of 0.48% and 0.14%, respectively,  $p < 0.001$ ). Age at diagnosis was  $41.1 \pm 18.8$  years and  $35.6 \pm 16.2$  years among the Jewish and Arab populations, respectively ( $p < 0.001$ ). Of these 1,056 (51.5%) Jewish patients and 132 (50.2%) Arab patients were women ( $p = 0.68$ ). BMI was similar among the Jewish and Arab patients ( $25.3 \pm 6$  and  $25 \pm 5.1$ , respectively) ( $p = 0.64$ ). CD was found in 1,070 (52%) of the Jewish patients and in 134 (51%) of the Arab patients, the rest had UC ( $p = 0.7$ ). The Arab patients had more anemia, hypoalbuminemia, hypocholesterolemia and disease exacerbations than the Jewish patients (Table 2). The Arab patients underwent fewer colonoscopies and bone density studies after diagnosis, but there was no difference in the percentage undergoing small bowel imaging between the two groups. The Arab patients had more IBD related hospitalizations than the Jewish patients (37.6% vs. 28%, respectively,  $p < 0.001$ ), but no difference was noted between the groups regarding IBD related surgery (Table 2). The Arab patients were treated more often with steroids (46% vs. 36.5%, respectively,  $p < 0.01$ ), but there was no difference between the two groups regarding treatment with 5ASA, immunomodulators, Budesonide or anti- TNF (Figure 1). Jewish patients had lower rates of diabetes, higher rates of dyslipidemia and thus received more lipid lowering drugs than Arab patients. No difference was noted between the two groups in terms of aspirin and NSAID's consumption (Table 1).

## Discussion

The present study demonstrated an increasing prevalence of IBD in both the Jewish and the Arab populations in Israel. However, important differences were noted between these two ethnic groups. The Arab population demonstrated lower prevalence, younger age at presentation, more exacerbations and hospitalizations and increased prescription of steroids. To the best of our knowledge, this study



includes the largest population studied in Israel on the topic of IBD [1,9,12,16]. The subjects studied belong to two stable ethnic groups living in the same area in Israel, with similar access to the same healthcare system. With this in mind, we think that the differences found between the two groups, can be explained by a combination of genetic differences and socio-cultural effects.

Traditionally, IBD is reported as more prevalent in developed countries with a north-to-south gradient [17]. However, in the last three decades, geographic distinction has become less prominent, with reports of high incidence of IBD in southern Europe and Australia [18-20]. Ethnicity is another important factor. IBD has been reported as more prevalent in Jews, especially those of Ashkenazi ancestry and less prevalent among other ethnic groups such as Arabs, Spanish, African- American and Chinese [7,9,21]. An increase in the overall incidence and prevalence of IBD is reported worldwide [22,23], with a concomitant increase among ethnic groups previously believed to be of low prevalence, such as Hispanics and Asians [24-26]. Past reports, have documented lower prevalence of IBD in Ashkenazi Jews in Israel compared to those in North America [27,28], and very low to zero prevalence among the Arab- Israeli population [9,10,11]. Other recent studies from Israel confirmed the increasing prevalence among the Jewish population [16] with continuing low prevalence in the Arab population [12]. The present study demonstrated an increasing prevalence of IBD among the Jewish population, approaching that reported in Europe and North America [26]. However, we also found increasing prevalence among the Arab- Israeli population, reaching 140/100,000 compared to 54/100,000 noted in a previous study [12]. These differences may be attributed, at least in part, to much smaller [16] and less homogenous [12] populations studied. The significant increase in the prevalence of IBD among the Arab population could be explained by Westernization of their life style, including improved sanitation, consumption of industrialized food, urbanization of the environment and increased availability of medical care [14,15,26].

Several previous studies have investigated IBD among various ethnic groups. [29-31]. These studies found differences in IBD phenotype, in the minority population, in terms of disease location, behavior and extra intestinal manifestations. The current study found that the Arab patients were younger at diagnosis and had more parameters indicating disease activity such as higher rate of anemia, hypoalbuminemia and hypocholesterolemia. In addition, they had, higher disease exacerbation rates, and more IBD related hospitalizations. While previous studies have compared either native to immigrant populations or patients living in different locations, we studied two native ethnic groups living in the same district in Israel who were exposed to the same health care system. Our findings suggest more aggressive disease among the Arab population, although lack of adherence to medical treatment and follow-up cannot be excluded.

Genetic variability has been noted in ethnic groups with IBD around the world [32-34]. Genetic differences between Jewish and Arab IBD patients in Israel were described by Karban, et al. [35,36]. They found a significantly lower rate of NOD2/CARD15 mutation and higher frequency of GSTT1-null in Arab compared to Jewish IBD patients. Although, the Jews and Arabs, observed in this study, originate from similar geographic areas, they share few genetic similarities [37]. This might explain the earlier onset of IBD in the Arab population.

In addition to environmental and genetic factors, we suggest that behavioral factors play a role in the differences found between the two populations. Recent studies have investigated the causes of lack of adherence to medical treatment in Arab populations both in Israel and North America. They found decreased compliance rate due to lower awareness of the disease and lack of access to medical care as well as cultural differences leading to reliance on traditional medications [38-40]. Low socioeconomic status has also been found to affect the effectiveness of IBD management [41]. The Arab population in Israel has, for the most part, a lower socioeconomic status than the Jewish population [14], supporting this theory. Fewer colonoscopies and bone-density spectrometrys among the Arab patients supports the lack of adherence theory. We found a higher rate of corticosteroid use and more IBD related hospitalizations in the group of Arab patients. Nevertheless, this group did not have a higher rate of IBD related surgeries. The higher steroid use, usually prescribed by the family physician as an urgent short term treatment, and the higher hospitalization rate may be secondary to lower compliance with long term medical therapy and follow up. Much disease exacerbation is treated during admission, hence the equal rates of surgery between the two groups.

Other than steroids, there was no difference in medications use including 5ASA, immunomodulators and anti- TNF, between the groups. Most studies report lower rates of immunomodulators and biologic therapy in IBD patients from minority ethnic groups [29,42,43]. Our findings support the basic assumption of equal access to medical attention among both populations.

The main limitation of this study is its retrospective nature, with potentially incomplete information. The disease activity was defined from laboratory data alone and not from the disease activity index, since the data was retrieved electronically from the laboratory information. However, this HMO database is one of the largest of its kind providing an opportunity to compare these two permanent, stable ethnically different populations who reside in the same geographic area.

In summary, this study compared large populations of Jewish and Arab IBD patients in Israel. Both ethnic groups are stable, live in the same area and have equal access to medical attention and facilities. The data for both populations support the global increase in IBD prevalence. This increase is occurring both in high prevalence populations and in an ethnic group once thought to have very low to no risk for the disease. We found a difference in disease phenotype manifested as more active disease in the Arab group. Apart from objective genetic and environmental differences, which should be further investigated, ethnic and cultural differences probably have a very important contribution. Our findings suggest that investing in medical education and close patient guidance by culturally sensitive

medical personnel can help achieve greater patients' compliance and better disease control.

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