Lerner and Matthias. J Clin Gastroenterol Treat 2017, 3:040
Volume 3 | Issue 1
ISSN: 2469-584X

Journal of
Clinical Gastroenterology and Treatment

Editorial: Open Access

One Size Doesn't Fit All: IBD in Arabs and Jews in Israel, Potential Environmental and Genetic Impacts

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Abstract

Inflammatory bowel disease (IBD) is influenced by genetic susceptibility and surrounding environmental factors. Despite unknown etiology, the environmental factors are continuously unraveled. Studying ethnical differences in a well characterized and stable region might disclose etiologies and pathophysiological mechanisms. The ethnical trends in IBD in Israel disclosed incidents, epidemiological, clinical, therapeutical and morbidity differences between the Arabs and Jews dwelling in a non-migrant, stable, Arab and Jewish distinct homogenous ethnic population districts. Interventions based on empowerment for medical care, cultural and behavioral elements presented in Arabic terms and concepts, improving nutritional habits and impacting lifestyle, can potentially minimize the IBD trends' gaps between those ethnicities.

Inflammatory bowel disease (IBD) is a frequent chronic inflammatory disease, comprising Crohn's disease (CD) and ulcerative colitis (UC). It affects the gastrointestinal tract but, many remote organs present extra-intestinal manifestations. Its etiology is unknown, its phenotypes is multi-faced, the epidemiology is changing, the genes involved are continuously unrevealed, reaching the number of 100 and the environmental factors are associative, far from presenting cause and effect relationship. Many environmental events were associated with IBD. Westernized lifestyle and habits, hygiene hypothesis, living in city, being a migrant, social class, smoking, microorganisms and infections, appendectomy, tonsillectomy, medication, nutrition and specific nutrients, breastfeeding and stress are some of them [1-4]. There are multiple strategies to explore the genetic/environmental interplay in IBD. Geoepidemiology [5], migration of populations [6] and ethnical analysis [7]. However, most ethnic comparisons originated in North America, comparing Caucasians to African, Hispanic, Indian and South/Pacific Asian, IBD populations [8-11]. Despite growing Arab communities in the western countries, non to my knowledge, characterized their IBD genetics, behavior and features. This is one of the reasons why Fabiana, et al. should congratulated for their comparative study, exploring differences between Arab and Jewish IBD patients in Israel [12].

Fabiana, et al. observed in the Arab IBD population a lower prevalence, younger age at diagnosis, more exacerbations, anemia, hypoalbuminemia, hypocholesterolemia, more oral steroid intakes, less colonoscopies and bone densitometries and more IBD related hospitalizations. Despite performing an observational comparative study, the authors concluded that their results "support the central role of the environment in the phenotypic expression of the IBD" [12]. Those differences can't be explain by the geoepidemiological North/South, west/east, developed/underdeveloped countries worldwide gradients [13], due to the small surface of the country and the well delimitated region of the Sharon-Shomron district.

Although the Arab minority in Israel live in the same geographical regions as the Jew, having the same broad basket of healthcare services, they practice different lifestyle, consume different nutrients, and exposed to different environmental factors. Following are some potential environmental dissimilarities between the two ethnic groups that might have impacted the differences in the IBD (Table 1).

Taken together, a wide environmental influences starting very early, from mode of childbirth and early-life exposures (including breastfeeding and antibiotic exposure in infancy) to later adult exposure (including smoking, stress, diet and lifestyle) could have impacted Fabiana, et al. results. Dietary fiber (fruits and vegetables), saturated fats, depression and impaired sleep, and low vitamin D levels have all been associated with IBD incidence.

Might the Differential Nutritional Habits Influenced the IBD Trends Between Arab and Jews?

A tight interaction exist between the gut microbiome/dysbiosis and IBD and they are nutrition depended [30-33]. Due to those cross-talks, a nutritional modulation of gene expression was suggested, lately, to benefit CD patients [33]. More so, nutritional deficiencies exist in IBD patients, inducing anemia, bone diseases, hypercoagulability, reduced wound healing and increased colorectal cancer risk [34]. Since adherence to Mediterranean diet is higher in the Arab populations and since the diet impacts gut microbiome and the associated metabolome [35,36], one wonders what their impact on IBD behavior are.

Intestinal microbiome, nutritional deficiencies and human health in general and IBD specifically are nutrition dependent. The nutritional Arab/Jewish discrepancies might have influenced the trends described by Fabiana, et al. [12] (Table 2).

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Citation: Lerner A, Matthias T (2017) One Size Doesn't Fit All: IBD in Arabs and Jews in Israel, Potential Environmental and Genetic Impacts. J Clin Gastroenterol Treat 3:040

Received: January 02, 2017: **Accepted:** January 05, 2017: **Published:** January 07, 2017

Table 1: Potential epidemiological and environmental dissimilarities among Arabs and Jews that might influence IBD trends in Israel.

Environmental factor	Arab	Jews	References
Doctor-patient relationship	Islamic medical ethics	International medical ethics	[14,15]
Smoking	High	low	[16-18]
Life expectancy	low	high	[18]
Obesity	high	low	[18]
Social inequality	lower	higher	[18]
Mortality & morbidity	higher	lower	[19,20]
Eating disorders	low	high	[21-23]
Weight/self-criticism concerns	higher	lower	[23]
Alcohol heavy consumption	higher	lower	[24]
Hospitalization rate for chronic disease	higher	lower	[25]
Economic difficulties→inadequate medical care	higher	lower	[25]
Faith in traditional therapy	higher	lower	[25]
Modesty, gender preference, illness causation misconceptions	higher	lower	[26]
Physical activity	low	high	[25]
Social trust, perceived helpfulness, trust in authorities, social support	low	high	[27]
Subjective reported health	high	lower	[28]
larger households, with tobacco smokers	high	lower	[29]
Breastfed	high	lower	[29]
Hospitalized and used antibiotics recently	high	lower	[29]

Table 2: Potential nutritional dissimilarities among Arabs and Jews that might influence IBD trends in Israel.

Nutritional factors	Arab	Jews	References
Nutritional counseling	low	high	[25]
Western diet	increasing	high	[25]
Mediterranean diet	higher	lower	[36]
Monounsaturated fatty acids	more	less	[36]
n-6 polyunsaturated fatty acids	less	more	[36]
Olive oil	more	less	[36]

IBD in the Arab Middle East

Before the spread of Islam, Arab referred to any of the largely nomadic Semitic people from the northern and central Arabian Peninsula. Since then many genetic, environmental, historical, migration, inter marriage and eco-events impacted the evolution of the Middle East Arab populations. The origin of the Israeli Arabs is difficult to trace but comparing surveys on IBD in neighboring countries might clarify some of Fabiana, et al. observations [12]. Studies have indicated a rise in the incidence of CD in Saudi Arabia, as well as in Kuwait with almost a five-fold increase in CD. If compared globally, IBD incidence and prevalence are up to 20-folds lower in the area than other locations in the world [37]. Interestingly, in addition to IBD incidence surge in Middle Eastern countries, a younger age on presentation, more males are affected, and less need for surgery and biological therapy, were noted in some of surrounding countries [37-44]. So, one can see some similarities between Israeli Arabs and other Middle East neighboring countries.

What is known from the Recent Literature on IBD in Arabs in Israel?

Fabiana, et al. [12], covered extensively the literature on the subject. A more recent survey among Bedouin Arabs in Southern Israel substantiates Lerner A, et al. results concerning increasing incidence, albeit, less than in the Jews, however, the Bedouin phenotype seems to be more aggressive. Higher % of patients was treated biologically and more needed surgery [45]. Righteously, the authors suggested association with the change in lifestyle and urbanization over previous decades. The Israeli IBD Research Nucleus group highlighted the effect of psychosocial stressors on IBD patients, but no segregation was studied between the majority and the minorities [46].

What about the Genetic Impact on IBD Behavior in the Arab Minority Compared to the Jewish Majority, in Israel

No doubt that the higher consanguinity among Israeli Arabs predispose them for chronic diseases with genetic background [47]. Unfortunately, only few genetic studies were performed on IBD predisposing genes in Israeli Arabs. NOD2/CARD15 is a major susceptibility gene for CD. In Israel Ashkenazi Jew have the highest carrier rate (47.4%), followed by the Sephardic Jews (27.45%) and the Arabs had the lowest one (8.2%) [48,49]. The genetic susceptibility follows their CD prevalence. This suggests that NOD2/CARD15 mutations have an important effect on CD prevalence within a specific population, but not on their ethnic phenotype. Extending the susceptibility to the entire world, those mutations are either rare or absent in Asian, African and Arab [50,51]. Another gene family involved in oxidant/antioxidant balance is the glutathione S-transferase enzymes: GSTM1 and GSTT1. Arab Muslims IBD patients have significantly higher SSTT1-null frequency, thus alluding to the genetic background importance in IBD [52].

It should be emphasized that no genotyping of geographically diverse Middle East Arab populations was performed, like recently in the Druze trios [53]. This and lake of environmental characteristics comparison of the 22 Arab Middle East countries, no doubt, weakens the interpretations and should be treated with a "grain of salt". The topic is further complicated by the fact that host–microbe interactions have shaped the genetic architecture of IBD [54], thus bringing up the evolutionary struggle between bags and us and the central role played by the intestinal eco-system events in shaping human gene functions and chronic diseases induction [55-57].

Conclusions

IBD is influenced by genetic susceptibility and surrounding environmental factors. The expanded susceptible genes surpassed 100 gene and the environmental factors are continuously unraveled. Studying ethnical differences in a well characterized and stable region might disclose etiologies and pathophysiological mechanisms. The Middle East is good candidate for such studies. The ethnical trends in IBD in Israel disclosed incidents, epidemiological, clinical, therapeutical and morbidity differences between the Arabs and Jews dwelling in central Israel. Interventions based on empowerment for medical care, cultural elements presented in Arabic terms and concepts, nutritional habits and lifestyle, can potentially minimize the IBD trends' gaps between those ethnicities.

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