Ethnic Background as a Risk Factor for Advanced Age-Related Macular Degeneration in Israel

Saleh Abu Asleh MD and Itay Chowers MD

Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel

Key words: age-related macular degeneration, Arabs, ethnic background, Jews, blindness

Abstract

Background: Age-related macular degeneration is the most common cause of legal blindness in the developed world including Israel. Ethnic background is a risk factor for advanced AMD in several populations, however the relative prevalence of this disease in different ethnic groups in the Middle East is unknown.

Objectives: To compare the prevalence of advanced AMD in Arabs and Jews in Israel.

Methods: We performed a retrospective analysis of two independent groups of patients: the first group comprised a sequential series of Jerusalem residents who underwent photodynamic therapy for neovascular AMD (PDT group), and the second group consisted of all individuals in Jerusalem who received a blind certificate due to AMD (legal blindness group). Control groups were assessed to exclude inherited ethnic associated bias in the two study groups.

Results: The PDT group included 146 patients: 142 were Jews (97.3%) and 4 were Arabs (2.7%). The legal blindness group included 340 Jerusalem residents: 326 Jews (96%) and 14 Arabs (4%). The number of Arab AMD patients in the two groups was lower than expected based on the ethnic composition of the age-matched Jerusalem population (P = 0.0002 for the PDT group, and P < 0.0001 for the legal blindness group). By contrast, the number of non-AMD Arab patients who were treated in the same clinic and the number of Arabs who received a blind certificate for diabetic retinopathy was not different from expected based on their relative number in the Jerusalem population.

Conclusions: Advanced AMD is less common in the Arab than the Jewish population of Jerusalem. Genetic and environmental factors may account for this difference. A population-based study is required to assess the overall prevalence of AMD in Jews and Arabs.

IMAJ 2007;9:656–658

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Ethnic background is believed to be a risk factor for age-related macular degeneration [1-3]. In the United States advanced AMD is more common in Caucasians compared to blacks and Mexican Americans, while the prevalence of earlier forms of the disease such as drusen and pigmentary retinal changes may be similar in these ethnic groups [2,4-8]. It was also shown that AMD accounts for a smaller relative number of legal blindness cases in blacks compared to whites [9,10]. The prevalence of AMD may also be lower in Japanese, Bantu blacks, and residents of Barbados, compared to Caucasians [11-14].

While the factors that underlie differences in the prevalence of AMD across ethnic backgrounds are still unclear, characterizing these differences may provide important epidemiological information as well as potential insight into the pathogenesis of the disease.

The Jewish and Arab populations in Israel are characterized by different prevalence of several chronic diseases [15] and it has been our clinical impression that relatively few individuals of Arab origin develop advanced AMD. To the best of our knowledge the relative prevalence of AMD in different populations in the Middle East in general and in Jews and Arabs in particular has not been previously reported. To address this issue we compared the prevalence of advanced AMD between Arabs and Jews in two independent groups of patients. The results from both groups suggest that advanced AMD is relatively uncommon in Arabs compared to Jews.

Patients and Methods

Two consecutive series of patients were included in the study. The first group (the PDT group) included a sequential series of Jerusalem residents over the age of 65 years who underwent photodynamic therapy for choroidal neovascularization secondary to AMD. AMD was diagnosed according to the AREDS criteria (Age-Related Eye Disease Study) [16]. All treatments were performed in the Department of Ophthalmology of the Hadassah-Hebrew University Medical Center in Jerusalem, Israel, between November 2004 and July 2005. During the study period this was the only facility that provided PDT for Jerusalem residents. A detailed history was taken and each patient was examined by a retina specialist. To assess if the patient population in our clinic as a whole (excluding AMD patients) is biased in terms of the relative number of Arabs and Jews compared to their relative number in the Jerusalem population we also evaluated a control group. This group included all Jerusalem residents over the age of 65 who underwent non-PDT ophthalmic laser therapy during the same time period in our clinic (i.e., yag capsulotomy and laser photocoagulation treatment for retinal vascular diseases or retinal breaks).

The second study group (blind certificate group) included all Jerusalem residents over the age of 65 who were registered as legally blind due to AMD in 2003 according to the records of the Ministry of Social Affairs (legally blind group). To exclude

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AMD = age-related macular degeneration
PDT = photodynamic therapy
potential ethnic background-associated bias (unrelated to AMD) in the blind certificate database we also analyzed the relative number of Arabs and Jews among individuals who received a blind certificate for diabetic retinopathy.

Demographic data on the population in Jerusalem were extracted from a report by the Jerusalem institute for Israel studies (Jerusalem: facts and trends 2002/3, http://www.jis.org.il). The chi-square approximation test was used to compare the relative number of Arab and Jewish AMD patients with their expected number according to the ethnic composition of the Jerusalem population.

Results

The PDT group included 146 Jerusalem residents over the age of 65 who received PDT for neovascular AMD: 142 (97.3%) were Jews and 4 (2.7%) were Arabs. During the same period, 199 patients underwent non-PDT ophthalmic laser treatments; 182 (91%) of these patients were Jews and 17 (9%) were Arabs. By comparison, in 2003 there were 55,400 people over the age of 65 living in Jerusalem: 48,000 individuals of this age group were Jews (87%), while 7400 (13%) were Arabs. A similar ethnic distribution was observed in the ≥ 75 year age group – of 24,400 individuals in total, 21,700 (89%) were Jews and 2700 (11%) Arabs.

The relative number of Arab AMD patients who underwent PDT was lower than expected according to their relative number in the Jerusalem population ($P = 0.0002$, chi-square approximation, relative risk 0.18, 95% confidence interval 0.066–0.488). The number of Arab patients undergoing other laser therapies was lower than expected, at a borderline significance level ($P = 0.052$). However, Arabs were more likely to undergo non-PDT laser treatments than PDT, as compared to Jews ($P = 0.038$).

The second study group consisted of Jerusalem residents older than 65 who became legally blind as a result of AMD. Of 340 such individuals, 326 (96%) were Jews and 14 (4%) were Arabs. In the same age group 90 individuals became blind as a result of diabetic retinopathy, 72 (80%) of them were Jews and 18 (20%) were Arabs. In this group, the number of Arab AMD patients was lower than expected according to their proportion in the age-matched population ($P < 0.0001$, chi-square approximation, RR 0.276, 95% CI 0.161–0.471), while the relative number of Arabs and Jews with diabetic retinopathy-associated legal blindness was not significantly different from the expected level ($P = 0.1$). Arabs were more likely to be legally blind due to diabetic retinopathy than to be blind due to AMD ($P < 0.0001$, RR 3.109, 95% CI 2.147–4.503). Analysis of the data from both groups for individuals who were ≥ 75 years showed similar findings (results not shown).

Discussion

This study shows that in Jerusalem, individuals of Arab origin are less likely to be treated with PDT and to receive blind certification due to AMD as compared to individuals of Jewish origin. Combined, these data from two different groups imply that advanced AMD is less common in Arabs than in Jews.

Several confounding factors should be taken into account when considering our findings. First, one could speculate that Jews may have better accessibility to PDT or blind certification compared to Arabs. This potential source of bias is unlikely since all Jewish and Arab residents of Jerusalem are covered by the same government-supported health insurance programs. PDT for neovascular AMD (both predominantly classic and occult lesions) is included in the mandatory “health basket” that each of the medical insurance carriers must provide. To further exclude this potential source of bias we analyzed control groups of age-matched, non-AMD patients for both the PDT and the blind certificate samples. This analysis demonstrated a significant smaller relative number of Arabs among patients with advanced AMD compared with the control groups. This finding further supports the conclusion that the relatively small number of Arab patients with advanced AMD recorded in this study is not the result of bias introduced by different accessibility to treatment.

Another potential bias source is that the different prevalence of other known risk factors for AMD among Arabs and Jews may lead to a lower prevalence of advanced AMD in Arabs. In that respect it should be stressed that our analysis took into account the effect of age, which is the most significant risk factor for AMD. The prevalence of other risk factors for AMD such as hypertension and smoking may vary among Arabs and Jews in Israel. Hypertension may be less common in Arabs while smoking may be more common among Arab males than Jewish males, but less common among Arab women than Jewish women [15,17]. However, based on the limited magnitude of hypertension and smoking as risk factors for AMD it is unlikely that these factors by themselves underlie our findings.

The decreased prevalence of advanced AMD in Arabs may be attributed to genetic background and environmental factors such as diet. For example, it was previously suggested that higher melanin content in the retinal pigment epithelium of dark-complexioned individuals may decrease the risk for oxidative injury and AMD progression [18]. While the validity of this hypothesis is still unclear, over 63% of our Jewish AMD patients in the PDT group were of Ashkenazi origin – having a fair complexion – compared to the Arab population. While complexion-associated differences in the prevalence of AMD among Jews of Ashkenazi and Sephardi origin* may also exist, we are unable to assess this possibility in the absence of information on the relative number of Sephardi and Ashkenazi Jews in Jerusalem.

The overall prevalence of AMD in both the Jewish and Arab populations in Israel is still unknown. In this respect it is important to note that while legal blindness due to AMD is rare in African-Americans [18], population-based studies such as the NHANES-III and the Barbados study reported that early AMD is common in blacks [3,12]. A population-based study is required to assess whether such prevalence patterns also characterize AMD in Arabs.

**RR** = relative risk
**CI** = confidence interval
* Ashkenazi refers to Jews of East European descent, and Sephardi to Jews of Middle Eastern or North African descent
References


Correspondence: Dr I. Chowers, Dept. of Ophthalmology, Hadassah-Hebrew University Medical Center, P.O. Box 12000, Jerusalem 91120, Israel.
Phone: (972-2) 677-7882, Fax: (972-2) 642-8896
email: chowers@md.huji.ac.il

Capsule

Target identification tool

A challenge for functional genomics has been to make meaningful global measurements of the interactions between transcription factors (and co-factors) and DNA. It has been difficult, especially in large genomes, to explicitly map individual binding sites and individual factor-target gene interactions. Johnson et al. have developed a combination of chromatin immunoprecipitation and ultrahigh throughput sequencing to achieve high specificity and 50 base pair resolution. This approach was used to study regulation by neuronal restrictive silencing factor (NRSF; also known as REST, for repressor element-1 silencing transcription factor) and identify targets of key positive regulators of pancreatic neuroendocrine development.

Science 2007;316:1497
Eitan Israeli

Capsule

Stem cells reprogramming

Early attempts in the 1980s to clone animals by transferring the nucleus of a somatic cell into a zygote failed, leading to a focus on doing the procedure with unfertilized oocytes. Human eggs, however, are difficult to obtain. Eggan and colleagues have shown that if nuclear DNA is removed from the dividing mouse zygote at just the right moment, it will successfully reprogram an introduced nucleus from a somatic cell. In this experiment, the researchers succeeded in creating both new lines of ES cells and apparently healthy cloned mice. This work suggests that to create patient-specific human ES cell lines, researchers could make use of fertilized eggs that would otherwise be discarded at fertility clinics, sidestepping the problematic issue of egg donation.

Science 2007;316:1404
Eitan Israeli