Race, Ethnicity and Prevalence of Primary Open-Angle Glaucoma

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Background: Recently, some authors pooled data from studies on the Dutch, Australians and Americans of European origin in an attempt to predict the prevalence of primary open-angle glaucoma (POAG) in the United States.

Purpose: To examine potential ethnic diversity in the prevalence of POAG among populations of the "same race."

Methods: Medical literature was searched, and 11 population-based studies on populations of African origin and five on populations of European origin were identified.

Results: The prevalence of POAG was significantly higher in white Australians than in the Dutch ($p<0.001$) and was significantly lower ($p<0.001$) among black populations in South Africa, Nigeria, Tanzania and the United States than in Ghana, St. Lucia or Barbados. Notably, the prevalence was significantly lower in Afro Caribbeans living in London than in St. Lucia or Barbados ($p<0.001$). There was, however, inconsistency in the definition of POAG among the different studies.

Conclusions: There is a wide range in the prevalence of POAG among populations of the same "race," which might be attributed to the different methodology and definition of POAG; potential difference in social, behavioral and environmental factors; and/or genetic predisposition. Scrutiny is warranted when pooling data from different ethnic groups of the "same race" in meta-analyses.

Key words: race ■ ethnicity ■ glaucoma ■ environmental ■ genetic

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It is well documented that the prevalence of primary open-angle glaucoma (POAG) is several folds higher in African Americans and Afro Caribbeans than in Caucasians.[1-3] The observed difference is often attributed to "race."[1-3] However, race in humans is a complex and controversial concept,[5-7] which involves anthropology, genetics, culture, religion, language, geographic locations, inhabitant environment, population history and political motives. It is unclear whether the observed difference in the prevalence of POAG is attributed to potential differences in environmental exposure, genetic predisposition or other factors. Recently, data derived from studies on Australians, Dutch and Americans of European ancestry have been pooled to predict the prevalence of POAG among whites in the United States.[4] Such an approach assumes uniform definition of POAG among studies and genetic homogeneity of race regardless of environment and ethnicity (a word derived from the Greek word *ethnos* meaning "nation" or "people"). The validity of using such pooled data has not been determined.

Studies have shown that there is a higher prevalence of POAG in individuals of African decent. The observed "racial" difference may not necessarily be due to genetics but rather to potential differences in social, behavioral and environmental factors. For example, there are apparent differences in general between Caucasian and African Americans in socioeconomic status, nutritional status, dietary habit, lifestyle, residential environment, medical conditions such as hypertension, diabetes and obesity, and access to healthcare and health insurance.[8-11] Such differences may exist among different ethnic groups of the same "race" as well, which may conceivably result in difference in the prevalence of diseases, such as POAG.

One of the first population-based studies in St. Lucia, West Indies showed a high prevalence of POAG among Afro Caribbeans ≥30 years of age (8.8%). Subsequent studies reported higher prevalence among African Americans (4.74%) and Afro Caribbeans in Barbados (7.0%) compared to Caucasians (1.29%).[2,3] The prevalence is significantly higher in Afro

Caribbeans than African Americans.[4] Other population-based studies on the prevalence of POAG in populations of Africa have been published more recently.[12-18] In this article, we systematically examine potentially significant differences in the prevalence of POAG among different populations of the same "race." Possible reasons for the observed potential differences in prevalence among populations of seemingly the same "race" are discussed.

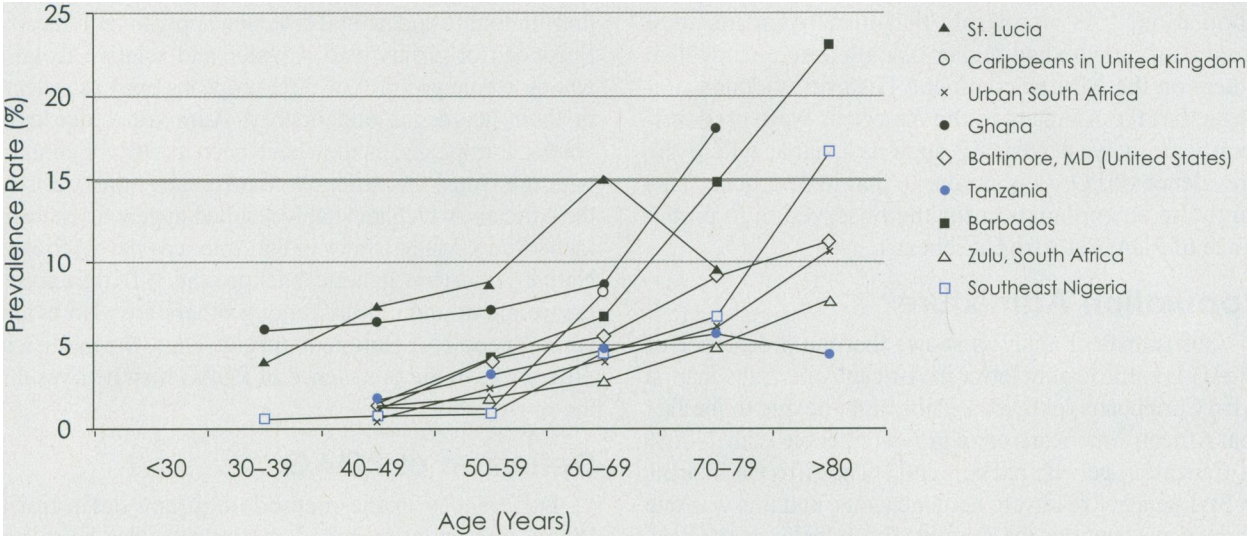
METHOD

Medline was searched with the key words "prevalence and glaucoma." Population-based studies on the prevalence of POAG[13-22] were identified and included in our analysis. In order to combine the results of these studies, Mantel-Haenszel Chi-squared test[23] was performed while adjusting for age. We avoided pooling samples even if they were from the same country. In most studies, subjects were stratified by age at a 10-year interval from 40– >80 years (Figure 1). Since three previous studies had also investigated subjects aged 30–39 years, we excluded this age group for comparison with studies that did not have such an age group. We combined ≥2 groups into a single "age >70" group and compared with studies that had only a group of "age >70." We also used data provided by the investigators of the studies[2,19-22] that were used by The Eye Disease Prevalence Research Group for their own meta-analysis.[4] Thus, the number of participants in this study is not necessarily the same as in the original, previously published studies.[2,19-22] Specifically, we converted the published[4] percentage into the number of participants in each age-group.[4] In order to keep the overall p value at level 0.05, Bonferroni's adjustment was used to account for multiple pair-wise comparisons between individual studies, and a p value of 0.001 was considered statistically significant. Potential difference in the definition of POAG in diagnosis was examined. Several studies had provided data of glaucoma suspects and other forms of glaucoma. In our statistical analysis, we included only those individuals with definite POAG.

RESULTS

We identified 11 population-based studies on the prevalence of POAG in subjects of African origin from eight countries—St. Lucia, the United States, England, Barbados, Ghana, Tanzania, Nigeria (three studies) and South Africa (three studies) (Figure 1; The study from Northern Nigerians is not included in the figure because of their use of a different set of age groups). We identified five population-based studies on Caucasians, which had been used to predict the prevalence of POAG in the United States by others.[4] The prevalence of POAG was significantly ($p<0.001$) lower in South Africa, Nigeria, Tanzania or Baltimore (MD, United States) than in Ghana, St. Lucia or Barbados ($p<0.001$). Notably, the prevalence was also significantly lower in Afro Caribbeans living in London than the Afro Caribbeans living in St. Lucia ($p<0.001$) and marginally lower ($p=0.007$) than those living in Barbados. There were no significant differences in sex distribution among these populations. Therefore, the difference was unlikely to be confounded by potential difference by sex. On the contrary, the prevalence of POAG was significantly higher in Australians (Sidney or Melbourne) than in the Dutch ($p<0.001$) and in white Americans ($p<0.001$). The prevalence was also marginally higher in Americans of European origin than in the Dutch ($p<0.005$ with Bonferroni correction taken into consideration). In some studies, cases were reviewed by a single eye specialist,[2]

Figure 1. The prevalence of POAG in African populations



while in others, by two.[1] There were various definitions of POAG among studies. Some used "cut-offs" for visual fields, intraocular pressure and cup-to-disc ratios.[21]

DISCUSSION

Our analyses show that there are statistically significant differences in the prevalence of POAG among populations of the same "race," i.e., populations either of African or of European origin. Several mechanisms may contribute to the observed significant differences.

Genetic Diversity among African Populations

Studies have shown that Africans are genetically the most diversified group in the world.[7,24] This conclusion is based on analysis of global haplotype patterns.[7,24] For example, East Asians, Europeans and other populations may lack certain alleles, while Africans in one region or another in sub-Saharan Africa tend to carry these alleles.[24] This suggests that Africa is not only the homeland of populations of the recent African diaspora but also the homeland of all modern humans.[25] Thus, it is not surprising that the prevalence of POAG is significantly different among African populations on the African continent. For example, this difference in prevalence is as high as 8.3% in Ghana[18] (similar to that of Afro Caribbeans[1]) or as low as 2.9% in rural northern Nigeria[15] and South Africa[16,17] (similar to certain Caucasian populations[20]).

Genetic Drift

Genetic drift occurs when a group of people who happen (by chance) to carry more or less alleles at certain genetic loci than in the original gene pool migrate to a different region, forming a new population with different allele frequencies. Millions of Africans "migrated"[25] to the Americas, and they might carry more of certain risk alleles for POAG than the original African population. It is also likely that these Africans were from a group who had higher risk allele frequency than others on the African continent. Historic evidence suggests that the Africans in the Americas were predominantly from West Africa,[25] such as Ghana, where the prevalence of POAG is similar to that in St. Lucia.[1] This might be an explanation for the observed high prevalence of POAG in Afro Caribbeans.

Population Admixture

Our statistical analysis shows that the prevalence of POAG is significantly lower in African Americans than in Afro Caribbeans ($p<0.001$). This might be due to the fact that African Americans are a group of people with 7–26% of Caucasian genetic background.[26] The Afro Caribbeans in St. Lucia are relatively homogeneous, and this was one of the considerations for choosing this population to investigate POAG prevalence in the 1986 survey.[1]

Environmental Exposure

The above analysis is based on the assumption that genetic factors play a predominant role in the observed difference in the prevalence of POAG among populations of the same "race," which deserves further investigation. We assume that the authors in previous studies used data derived from the Dutch and Australians to predict the prevalence of POAG in the United States[4] because of the presence of people of Dutch and Australian ancestry in the country. Even if they account for a larger proportion of the U.S. population, environmental exposure and other risk factors may conceivably modify the prevalence of POAG. For example, the prevalence of POAG in Caribbeans living in London is significantly lower than in those living in St. Lucia and is marginally lower than those living in Barbados. In addition to natural environmental factors (such as sun exposure and proximity to the equator), potential difference in social economic status and other nongenetic factors may have contributed to the difference in the prevalence of POAG. Evolutional forces, such as genetic drift, should also be considered in this argument. Finally, potential genetic predisposition might interact with environmental exposure, resulting in different prevalence (i.e., a risk allele may be manifested more vigorously in one environment than in another). The same argument can be made when we observe that populations living in the tropical (i.e., Africans) or subtropical (Asian Indians) regions have developed dark skin during evolution as a protection against excessive UV light. As these individuals migrated to countries of higher latitude with less sun exposure, they often failed to adapt themselves to the new environment, such that serum 25-hydroxyvitamin D fell below its optimal level,[10] which, in turn, resulted in pathological changes only in the new environment.

Genetic Diversity among Europeans

The aforementioned environmental factors and evolutional forces such as genetic diversity, genetic drift, population admixture and natural selection apply to individuals of European origin as well. Cluster and relative isolation among ethnic groups[27] of the Europeans exist as reflected in their languages and history. Admixture also exists among Europeans, as they have been at war for centuries with the Huns, the Mongols, the Persians, the Arabs and the Africans, which inevitably resulted in genetic exchange (gene flow). Many whites in the Americas have African or Native-American genetic background.[28] Differences in environment and culture among others are also evident among people of European origin. Thus, the significant differences in the prevalence of POAG may be a result of the above factors.

Definition of POAG

Differences in the methodology and definition of POAG in population-based studies may also be responsible for the observed ethnic differences in the preva-

lence of the disease. This makes it very difficult to predict the prevalence of POAG in one country based on data derived from studies in other countries. In addition, the results and observed difference in the prevalence of POAG among different ethnic groups should be interpreted with caution. Thus, there is a need for international consensus in the definition of POAG in epidemiologic studies.

Implications

The apparently significant difference in the prevalence of POAG among populations of the same "race" supports the notion that the common classification of race into Africans, Caucasians and Asians is inadequate in genetic studies of human populations.[7] Thus, using "pooled data from these large, worldwide population-based studies" may not "determine more precisely the magnitude of the problem in the United States."[4] Therefore, the predicted prevalence of POAG in the United States may be misleading. From a statistical point of view, heterogeneity is one of the major concerns in meta-analysis, and one should avoid pooling different populations for a statistical "advantage" of a larger sample size.

We acknowledge the fact that the concept of race/ethnicity has some usefulness in biomedical research and clinical medicine. However, there is a note of caution, since the initial racial classification was partly driven by political and social considerations."[5,6] We need to identify the underlying genetic as well as environmental factors, which may promote our understanding of the etiologies of diseases for effective diagnosis, treatment and elimination of health disparities. Many risk factors are environmental, social and behavioral, which might be more readily overcome by "environmental solutions,"[29] as may be the case with obesity.[29] We still face a great challenge in identifying these potential risk factors, some of which may be operational in the observed ethnic differences in the prevalence of POAG.

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