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Four-year incidence of Open-angle Glaucoma and Ocular Hypertension: The Los Angeles Latino Eye Study

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Glaucoma is second only to cataract as a cause of blindness worldwide.[1] In contrast to the blindness caused by cataract, glaucoma-related blindness is irreversible. It is estimated that 66.8 million persons in the world have open-angle glaucoma (OAG), and more than 3 million Americans are projected to be affected by this disease by 2020.[1;2] Given the increasing prevalence of OAG with aging, the demographic shift toward older populations in both developed and developing countries will lead to substantial increases in the incidence of OAG, which will undoubtedly become a challenging public health issue in the upcoming decades.

Numerous population-based studies have reported the prevalence of OAG.[3-9] Compared with cross-sectional studies, incident studies are more robust in elucidating risk factors for developing OAG and providing evidence for guidance of clinical management of OAG. However, few studies have documented incidence of OAG and no population-based studies have documented the incidence of OAG and OHT in the US. This lack of studies is mainly due to the difficulties inherent in conducting a long-term follow-up of a sizable population cohort, given the relatively low frequency of OAG in most populations. To date, all population-based longitudinal studies on OAG were performed outside the US among persons of African ancestry[10;11] and non-Hispanic whites.[12-14] As far as we are aware, no incidence data on OAG has been reported for Latinos. As the largest and fastest-growing minority in the US, Latinos have unique demographic, socioeconomic, and ocular health characteristics compared with other racial groups in the US.[15] Longitudinal studies on OAG in this population to assess the burden of this blinding disease are therefore important for establishing appropriate clinical and public-health intervention strategies.

In 2003, we reported the prevalence of OAG and ocular hypertension (OHT) in a population-based sample of Latinos in Los Angeles County, California. The prevalence of

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"Supplemental Material available at AJO.com"

OAG among Latinos was similar to that of African-Americans, yet much higher than that of non-Hispanic whites.[7] In this paper, we describe the incidence rates of OAG and OHT derived from the 4-year follow-up examination of this population. We also describe the longitudinal changes in structural and functional characteristics in eyes that develop OAG and OHT.

MATERIALS AND METHODS

STUDY POPULATION

The Los Angeles Latino Eye Study (LALES) is a population-based cohort study of eye disease in self-identified Latinos aged 40 years and older living in 6 census tracts in the city of La Puente, Los Angeles County, California.[16] Latinos (Hispanics, Hispanic Americans, and Latino Americans) are individuals who are born into or have descended from a Spanish-speaking community, regardless of race. In the United States they are a heterogeneous group, with the majority of Mexican ancestry (66%). Baseline examination was performed from 2000 to 2003 with 4-year follow-up examination from 2004 to 2008. Details regarding study design, methods, and baseline prevalence data have been reported elsewhere.[16]

INTERVIEW AND EXAMINATION PROCEDURES

All eligible participants from the baseline LALES examination were invited to return for a home interview and a clinical examination. Similar questionnaire and examination procedures were used for both baseline and follow-up studies. Trained ophthalmologists and technicians performed a comprehensive ocular examination using standardized protocols, which included visual field (VF) testing, Goldmann applanation intraocular pressure (IOP) measurement, and simultaneous stereoscopic fundus photography of the optic disc.

VISUAL FIELD EVALUATION

Detailed descriptions of all OAG/OHT diagnosis-related tests and definitions have been previously reported.[7] In brief, for VF evaluation, a Swedish Interactive Threshold Algorithm (SITA) Standard C24 was first performed in each eye. If the results were normal, no further tests were conducted. If the results were abnormal or unreliable, the tested eye would undergo a repeat VF test. No VF tests were performed on eyes that presented with visual acuity of light perception or worse. Next, two glaucoma specialists evaluated the field loss pattern and the congruence among all the repeated VF tests for the eye. Finally, based on an optic disc evaluation, clinical examination data review, and fundus photograph assessment, the glaucoma specialists determined if the field loss was characteristic of glaucoma, compatible with glaucoma, due to other neurological/non-glaucomatous cause or artifact, or not determined/not applicable.

OPTIC NERVE EVALUATION

For optic nerve evaluation, simultaneous stereoscopic optic disc photographs were evaluated using a stereoscopic viewer (Asahi viewer, Pentax, Englewood, Colorado, USA). The two glaucoma specialists first determined the photo quality. If the photograph was gradable, the appearance of the optic disc was characterized in terms of vertical and horizontal cup-disc ratio (CDR), CDR asymmetry between fellow eyes, disc and peripapillary nerve fiber layer hemorrhage, peripapillary atrophy (PPA), diffuse thinning of the neural rim, and notching of the neural rim. Finally, the optic disc was classified into the following categories: characteristic of glaucoma, compatible with glaucoma, abnormal but non-glaucomatous (optic disc abnormalities which are not characteristic of or compatible with typical glaucomatous changes, such as changes associated with ischemic optic neuropathy, congenital optic disc pits, laser photocoagulation), normal, or unsure (media opacities

precluded an accurate assessment of the optic disc from either disc photographs or on direct ophthalmoscopy). In the absence of clear, high-quality photographs, data from the direct binocular ophthalmoscopic examination of the optic nerve were used.

DIAGNOSIS OF OPEN ANGLE GLAUCOMA AND OCULAR HYPERTENSION

An expert consensus method was used for OAG diagnosis based on history and clinical examination data. A 3-step process was used to determine the OAG diagnosis. First, two glaucoma specialists evaluated all clinical history and examination data including VA, Van Herrick test results, gonioscopy results, evaluation of anterior and posterior ocular segments, clinical optic disc and fundus evaluation, optic disc photographs, and VF results. Second, the two specialists determined the presence or absence of OAG using specific guidelines. The two specialists graded both optic disc photographs and VFs independently and masked to each other. In determining the diagnosis of glaucoma, the specialists classified each eye of each person with particular consideration to the optic disc photographs and VFs. A diagnosis was assigned to each eye if both graders agreed. In the event of disagreement, a third glaucoma specialist assessed the data. An agreement between 2 of the 3 specialists was used to assign the eye. Additionally, the principal investigator (RV) performed a confirmatory review of all cases diagnosed as OAG.

The detailed diagnosis criteria for OAG are described elsewhere.[7] Briefly, based on the presence or absence of optic disc damage, VF defects, or both, as well as the degree of compatibility of these changes with glaucoma, the diagnoses were classified into definite glaucoma, and probable glaucoma. Incident OAG was defined as the presence of an open angle and a glaucomatous VF abnormality and/or evidence of glaucomatous optic disc damage at the 4-year follow-up examination in persons who did not have any evidence of glaucomatous VF abnormality and/or evidence of glaucomatous optic disc damage at baseline. Ocular hypertension was diagnosed in individuals with an IOP of > 21 mmHg (or ≤ 21 mmHg if the person was using OHT medications or had undergone IOP-lowering laser or incisional surgery in that eye), and the absence of both optic disc damage and abnormal VF tests results.

Incidence of OAG in this study is presented using 3 different approaches: 1) Incidence in the first eye required that both eyes were free of OAG at baseline. Participants were at risk of developing OAG in either eye or both eyes at follow-up; 2). Incidence of OAG in the second eye required that at baseline only one eye had OAG 3) Incidence of OAG in either eye was obtained by combining incidence of OAG in the first eye and the second eye. Similar approaches are used for presenting incident OHT data.

DATA AND STATISTICAL ANALYSIS

All clinical and grading data were entered into a central database with internal, automated, quality-control checks. Incidence and progression of OAG/OHT were dichotomized into yes/no categories. Comparisons of incidence rates were made across age groups. Age at baseline was categorized into 5 groups (40-49 years, 50-59 years, 60-69 years, 70-79 years, and 80+ years). Demographic and glaucoma-related clinic characteristics between baseline and follow-up examinations were compared using X^2 test for categorical variables and Student's *t* test for continuous variables. Associations of incidence rates across age groups were tested by the Mantel-Haenszel trend test. In addition, the crude overall incidence rates were age-adjusted to the LALES study cohort using direct standardization methods. Results were also annualized to enable comparison across other population-based studies. Inter-grader and intra-grader agreements were assessed in a random sample of eyes using weighted kappas. Secondary analyses included: 1) determining the frequency of specific diagnostic criteria for defining OAG; 2) comparing optic disc and clinical characteristics

between baseline and follow-up in participants with incident glaucoma or OHT; and 3) using prediction models to estimate the incidence of OAG or OHT in participants without a 4-year follow-up examination. The Statistical Analysis System (version 9.1, SAS Institute Inc, Cary, North Carolina, USA) was used for statistical analyses, conducted at the 0.05 significance level.

RESULTS

A flowchart assessing the analytical cohort is presented in Figure 1 (Supplemental Material at AJO.com). Of the 5907 living eligible participants with clinical examination data at baseline, 4538 (76.6%) completed the 4-year follow-up in-clinic exam. The mean (±SD) follow-up period was 4.3±0.03 years. The mean (±SD) age of participants was 54.7±10.5 years. Sixty percent of follow-up participants were female, and 76% were born outside of the United States. The participants identified their countries of origin as Mexico (64%), US (24%), El Salvador (5%), Guatemala (2.5%), Nicaragua (1%) and other (3.5%).

Complete and reliable glaucoma data were available for 3939 participants at both baseline and 4-year follow-up. Of the 599 participants who had a clinical examination but were without complete data for glaucoma diagnosis, 398 (66.4%) had ungradable fundus photos at follow-up, 118 underwent in-home examination (19.7%), 48 refused dilation (8.0%), 2 were physically unable to comply with the examination (0.3%). The reason for incomplete data was unknown for 33 (5.5%) participants. Therefore, the analysis cohort for this paper comprised the 3939 participants with valid data for OAG diagnosis in at least one eye at follow-up.

As shown in Table 1, compared with nonparticipants and those who were excluded for analysis (n=1968), participants in this analysis cohort (n=3939) were older (P=0.002) and were more likely to be married (73.5% vs. 70.7%, P=0.03), to have health insurance (67.2% vs. 56.8%, P<0.0001), to have at least 2 systemic co-morbidities (41.7% vs. 35.2%, P<0.0001), and to report a history of systemic hypertension (30.1% vs. 26.8%, P=0.01). There were no significant differences between these two groups in terms of gender distribution, country of origin, employment status, income and education level, and history of ocular diseases, including cataract, glaucoma, macular degeneration (MD), and diabetic retinopathy (DR) (P>0.05). Considering the big sample size of this study, the difference in age and marital status between participants and nonparticipants may not have an obvious impact on the prevalence estimation despite the statistically significant P values. Nevertheless, the significant differences between the two groups for the rate of comorbidities as well as for those with arterial hypertension should be considered when assessing the risk factors of OAG/OHT.

FOUR-YEAR INCIDENCE OF OPEN ANGLE GLAUCOMA AND OCULAR HYPERTENSION

For the 3939 participants with complete and valid glaucoma diagnosis data, the 4-year incidence of OAG in the first eye (among those without OAG at baseline) was 2.3% (95% CI, 1.8%-2.9%) (Table 2). The incidence in the second eye (among those who had OAG in one eye at baseline) was about 6-fold that in the first eye, with 11 of 91 persons (12.1%, 95%CI, 5.4%-18.8%) developing OAG after 4 years. When combining the incidence in either eye, 98 (2.5%) (95%CI, 2.0%-3.0%) were found to have developed OAG at the 4-year follow-up examination. After adjusting for the age distribution of this cohort, the overall age-standardized incidence of OAG was 2.5% (95%CI, 1.9%-3.0%) for the first eye group, 10.9% (95%CI, 4.5%-17.4%) for the second eye group, and 2.6% (95%CI, 2.1%-3.2%) for the either eye group. The incidence of OAG was higher in older Latinos than in younger ones. For the first, second, and either eye groups, the OAG incidence was 14-, 2.4-, and 15-fold higher in the oldest age group (≥80 years) relative to the youngest age group (40-49

years). No gender difference was found in the incidence of OAG in each group (P>0.05). Of the 87 participants who had incident OAG (iOAG) in the first eye, 23 (26.4%) had bilateral OAG and 64 (73.6%) had unilateral OAG.

Incident ocular hypertension in the first eye was present at the 4-year follow-up in 124 of 3589 participants (3.5%, 95CI, 2.9%-4.1%) (Table 3). The incidence in the second eye, however, was 31.2% (24/77, 95%CI, 20.8%-41.5%), about 10 times that of the first eye. Combining both eyes, there were 148 of 3666 persons (4.0%, 95%CI, 3.4%-4.7%) who had OHT at 4-year follow-up. Similar to OAG, there was a higher incidence of OHT in older Latinos than in younger Latinos (*P* for trend<0.001). Compared to the rate of iOHT in the youngest group of Latinos (40-49 years), the rate in the oldest group (≥80 years) was 3.7 times greater in the first eye group, 2.5 times greater in the second eye group, and 5.8 times greater in either eye group. After adjusting for the age distribution of LALES cohort, the overall 4-year incidence of OHT was 3.6% (95%CI, 2.3%-4.2%) for the first eye group, 29% (95%CI, 17.4%-40.6%) for the second eye group, and 4.2% (95%CI, 3.5%-4.9%) for the either eye group. No gender differences were found in OHT incidence for either group (*P*>0.05). Of the 124 participants with iOHT in the first eye, 70 (56.5%) had bilateral iOHT and 54 (43.6%) had unilateral iOHT.

COMPLETION AND REPRODUCIBILITY OF DATA COLLECTION FOR GLAUCOMA CLASSIFICATION

Of the 98 participants with iOAG, 94 (95.9%) had optic disc examination, 83 (84.7%) had gradable optic disc photographs, and 4 (4.1%) had no optic disc data. Two or more VF tests were performed on 54 (55.1%) participants, while 39 (39.8%) had 1 VF test, and 5 (5.1%) had no VF data (Table 4). The agreement between the 2 glaucoma specialists in estimating glaucoma-related parameters was substantial for vertical CDR (weighted k, 0.7 [95% CI, 0.5-0.8]), horizontal CDR (weighted k, 0.7 [95%CI, 0.5-0.9]) and judgments of abnormal VF tests (weighted k, 0.9 [95%CI, 0.8-1.0]). The agreement between two specialists in the diagnosis of OAG and OHT was 89.1% and 75.7% respectively.

CRITERIA FOR DIAGNOSIS OF OPEN ANGLE GLAUCOMA AT FOLLOW-UP EXAMINATION

Table 5 details the frequency of cases in each specific diagnostic criterion. Of the 98 participants with iOAG, 55 (56.1%) had at least one eye with both VF loss and optic disc damage, irrespective of IOP. Of the remaining participants, 14 (14.3%) were diagnosed with OAG in at least one eye based on a combination of VF defect and optic disc damage compatible with glaucoma; 29 (29.6%) had at least one eye diagnosed with OAG with either VF defect (n=9 [9.2%]) or optic disc damage (n=20 [20.4%]) that was characteristic of or compatible with glaucoma.

CHARACTERISTICS OF OPEN ANGLE GLAUCOMA AND OCULAR HYPERTENSION BETWEEN BASELINE AND FOLLOW-UP EXAMINATION

Details of the comparisons of clinical characteristics related to OAG and OHT between baseline and follow-up are summarized in Table 6 and Table 7, respectively. Only data from persons who had iOAG/OHT in the first eye and without glaucoma or OHT-related treatments were analyzed. At follow-up examination, participants with iOAG were more likely to have 1) more severe VF test defect in terms of mean defect (-5.2±7.2 at baseline vs. -5.8±6.9 at follow-up, P=0.002) and pattern standard deviation (3.3±2.6 vs. 4.1±2.6, P=0.001); 2) to have larger horizontal (0.5±0.1 vs. 0.6±0.1, P<0.0001) and vertical (0.5±0.1 vs. 0.7±0.1, P<0.0001) CDR; and 3) to have horizontal (1.1% vs. 16.1%, P=0.002) or vertical (1.1% vs. 36.8%, P<0.0001) CDR of > 0.7 compared with baseline results (Table 6). Among the participants with iOAG, 11.5%, 18.4%, 8.0% and 58.6% had horizontal, vertical CDR asymmetry of ≥ 0.3, diffuse thinning of neural rim to disc margin and notching of

neural rim respectively at follow-up, whereas none of the participants presented with these optic disc characteristics at baseline. No significant differences were detected for mean IOP (16.5±5.1mmHg vs. 16.2±5.2mmHg, P=0.82), proportion of IOP > 21 mmHg (15.1% vs. 15.1%, P=0.76), central corneal thickness (CCT) (547.3±43.5 μm vs. 547.1±44.3 μm, P=0.84), disc/nerve fiber layer hemorrhage (1.1% vs. 2.3%, P=0.56) and PPA (62.1% vs. 73.6%, P=0.09) between baseline and follow-up examinations among participants with iOAG.

On average, participants with iOHT were younger than those with iOAG (62.3±10.2 years vs. 67.1±11.6 years, P=0.002). Compared with baseline results, participants with iOHT had higher IOP (23.2±2.5 mmHg vs.16.8±2.5 mmHg, P<0.001) and thinner central cornea (563.4±29.5 μm vs. 558.2±31.2 μm, P=0.002) and were more likely to have PPA (33.9% vs. 60.5%, P<0.0001) at follow-up examination (Table 7). Visual field defect and CDR did not differ between baseline and follow-up examinations among these participants. No eyes were found to have optic nerve damage, including horizontal or vertical CDR > 0.7, CDR asymmetry ≥ 0.3, disc/nerve fiber layer hemorrhage, diffuse thinning of neural rim to disc margin or notching of neural rim, CDR>0.7 or CDR asymmetry ≥ 0.3. Two participants with iOHT (1.6%) were observed with disc/nerve fiber layer hemorrhage at the follow-up examination.

DISCUSSION

The Los Angeles Latino Eye Study is the first longitudinal study to provide incidence data on OAG and OHT in a large, well-defined cohort of adult Latinos.

In our study, the crude overall incidence of OAG at 4-year follow-up was 2.54% and 2.64% after adjusting for the age distribution of the LALES cohort. The OAG incidence is higher than that noted in non-Hispanic whites in Melbourne (1.1%/5 years, 0.22/year)[14] and Rotterdam (1.8%/5 years, 0.36%/year),[12] yet lower than that noted in blacks in Barbados (4.3%/4 years, 1.08%; 9.4%/9 years, 1.04%) (Table 8).[10,11] These discrepancies could be attributable to many factors, with racial group being critical. As reported in LALES baseline studies,[7] the OAG prevalence in Latinos is intermediate between that of the non-Hispanic whites and blacks, with the latter having the highest reported OAG prevalence. The consistent finding of interethnic variation of OAG incidence confirmed the important role of ethnicity in OAG development and the possible genetic susceptibility to this disease. Recent genome-wide association studies have identified certain loci associated with glaucoma-related characteristics among both Caucasians[17] and blacks.[11] Such genetic studies among Latinos are critical to further elucidate these hypotheses.

Differences in methodology across studies are not negligible when interpreting the results of comparison. However, this is less likely to account for the discrepancy between our results and that of the previous studies. The current study used a standardized protocol comparable with prior studies, including the examination of VF and optic disc and the results evaluation, the diagnostic criteria of glaucoma, and the definition of incidence. Although the definitions of probable glaucoma may vary slightly across studies, the definite glaucoma is defined consistently among these studies. The incidence of definite glaucoma in our study was 1.42%/4 years (55/3863), which was higher than that of the non-Hispanic whites in the Melbourne study[14] (0.5%/5 years) and the Rotterdam study[12] (0.6%/5 years) but lower than that of the blacks in the Barbados study (2.2%/4 years and 4.4%/9 years).[10;11] Finally, given the increasing prevalence of OAG with aging, the age range of the cohort and follow-up period could have a potential influence on the incidence rate. As shown in Table 8, the majority of prior studies were performed among persons aged 40 years and older, and in the

Rotterdam study,[12] participants were 55 years and older. Incidence of OAG in this study will be expected to be even lower if adjusted to an age range of ≥ 40.

Higher IOP is a well-established predictor for OAG development.[18;19] We found 4.03% of the participants developed OHT at the 4-year follow-up, indicating these individuals will be at risk to develop OAG in the future. However, given the higher CCT identified in these participants with iOHT, it is noted that the high measured IOP of a considerable portion of these participants may be due to a thicker cornea. Future follow-up over longer time, particularly the observation of VF and optic disc morphologic change, will provide important data on the accumulative effect of OHT to glaucomatous optic nerve damage.

The incidence of both OAG and OHT increased with age in our study. In Latinos aged 80 and older, the incidence of OAG was 15-fold that of Latinos 40-49 years old. This finding supports observations in previous studies.[10-12;14] The absence of gender difference in OAG incidence also confirmed prior studies: although males tend to have higher OAG incidence than females, the difference was not statistically significant.[10;12;14]

At the 4-year follow-up examination in our study, normal fellow eyes of OAG eyes identified at baseline had a 5-fold higher risk for having OAG compared with the fellow eyes of normal eyes. This is consistent with the results from Rotterdam study in which the 5-year incidence of OAG in the fellow eye of participants with prevalent OAG in one eye was 5 times higher than in the fellow eyes of non-OAG eyes.[12] We also found that 26.4% of the participants with iOAG in the first eye developed bilateral iOAG during the four years. These findings underscore the importance of observing and following up on the normal fellow eyes in the clinical management of patients with a first eye diagnosed with OAG. Considering the irreversible nature of glaucoma damage to the optic nerve, preservation of visual function of the fellow eye in OAG patients with one eye already affected also has crucial significance to health-related quality-of-life.

Compared with baseline results, participants with iOAG had significant deterioration in their VFs, CDR and CDR asymmetry between two eyes. Significantly more persons developed diffuse and localized thinning (notching) of the neural rim. These findings highlight the importance of these characteristics in OAG diagnosis and severity evaluation. In our study, the optic disc characteristics that differed most between follow-up and baseline examinations among participants with iOAG was notching of the neural rim. More than half of the participants with iOAG developed notching in at least one eye. This agrees with the findings of the Blue Mountain Study, in which neural rim notching had both good sensitivity and a positive predictive value for glaucoma.[20] Our finding also underscores the importance of neural rim notching in early diagnosis of OAG. When comparing the clinical features between follow-up and baseline examinations among participants with iOHT, no significant differences existed in the proportion of CDR>0.7, CDR asymmetry ≥ 0.3, disc/nerve fiber layer hemorrhage and in VF results. Only PPA was more common in eyes with iOHT compared to those without iOHT.

PPA has been suggested as a marker for persons at risk of converting from OHT to manifest glaucoma[21] and in identifying those with manifest glaucoma who are at risk for visual field deterioration.[22,23] Compared with baseline optic disc characteristics, a significantly higher proportion of participants with iOHT had PPA at follow-up compared to normal participants. However, persons with incident OAG were not more likely to have PPA compared to baseline. Our results indicate that although being a feature associated with glaucomatous optic nerve damage, PPA is not necessarily a pathognomonic sign of incident glaucoma.

Disc/nerve fiber layer hemorrhage was the optic nerve characteristic that showed the least change and was also identified in the fewest cases at follow-up examination among participants with iOAG. One possible reason may be that disc hemorrhages are transient and that photographs taken at follow-up may not record all the hemorrhages that may have occurred during the development of optic nerve damage.[24]

Thinner CCT is a powerful predictive clinical characteristic for the development of OAG.[25] In our study, participants with iOHT had a thicker cornea than participants with iOAG at both baseline and follow-up examinations ($P<0.001$). This may be attributable to the higher measured IOP in participants with thicker corneas. It is interesting that during follow up, we found a 1.3-μm decrease of CCT per year among participants with iOHT, however, no such longitudinal thinning of cornea was detected in participants with iOAG. These differences are small and may not be clinically meaningful.

Strengths and limitations

The 4-year follow-up study of LALES was based on a population with a large sample size and a high participation rate (76%). When assessing the incidence of OAG and OHT, standardized protocols were used, including those for determining glaucoma, obtaining simultaneous stereoscopic photographs of the optic disc, and performing VF tests (particularly for the confirmation of VF defects) with ≥ 2 threshold VFs. The diagnoses of glaucoma were performed independently by two glaucoma specialists, with a third glaucoma specialist adjudicating discrepancies. We also have relatively complete data for OAG diagnosis. These methods have allowed us to obtain an accurate estimate of the incidence of OAG/OHT comparable to previous studies.

Some limitations also need to be considered when interpreting the results and conclusions of this study. First, participants included in analysis group were more likely to have arterial hypertension than those who were excluded from the analysis. Given the potential positive association of arterial hypertension with OHT, the incidence OHT may be overestimated. However, a careful statistical analysis suggested that the imputed incidence rate of OAG/OHT for nonparticipants (using baseline data and adjusting for diabetes mellitus and arterial hypertension) was 2.3% (95%CI: 2.0%-2.6%)/3.12% (95%CI: 2.77%-3.46%), which is comparable to the actual observed incidence for participants, and the two groups do not differ in a meaningful manner. Second, the exclusion of institutionalized persons (nursing homes, group homes) may have led to underestimation of the OAG and OHT incidence as persons residing in such facilities tend to be older. Yet considering that Latinos are less likely to institutionalize their parents, the bias to the overall incidence rates from excluding such individuals may not be significant. Third, the study population are primarily Mexican Americans. Therefore, the results of our study may not be generalizable to all Latino subgroups. Finally, there is the possibility of a design effect since the analysis assumes independence between participants. However, we could not previously demonstrate evidence of a family clustering effect in the prevalence study; and thus, it is likely that any design effect present in this study is negligible.[7]

In summary, Latinos with a predominantly Mexican ancestry in Los Angeles have an incidence of OAG lower than that of US blacks and higher than that reported for non-Hispanic whites. Incidence of both OAG and OHT increases with advanced age. With the aging of the Latino population and its rapid growth, it is imperative to establish appropriate public health care strategies and effective clinical intervention in this and similar populations. Future population-based studies on risk factors for incident OAG and OHT are needed to determine the generalizability of our results in other racial ethnic groups and in other geographic areas.

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Table 1

Comparison of socio-demographic and clinical characteristics at baseline between participants and nonparticipants in the Los Angeles Latino Eye Study 4-year follow-up study.

	Analysis cohort[a] (N=3939)		Nonparticipants or Excluded[b] (N=1968)		
Characteristics	**n**	**%**	**n**	**%**	***P Value*[c]**
Gender (female)	2355	59.8	1130	57.4	0.09
Age group at baseline(yrs)					
Mean age at baseline (±SD)	54.6±10.3		53.7±10.9		0.002
40 to 49	1485	37.7	857	43.6	
50 to 59	1244	31.6	582	29.6	
60 to 69	809	20.5	324	16.5	
70 to 79	342	8.7	157	8.0	
80+	59	1.5	48	2.4	
Born in the United States	921	23.4	436	22.2	0.32
Acculturation (low |<1.9|)[d]	2640	67.0	1343	68.5	0.31
Working status (employed)	1988	50.5	1003	51.0	0.70
Education level ≥12 yrs	1347	34.2	626	31.8	0.08
Marital status (married)	2896	73.5	1391	70.7	0.03
Annual income> $40,000	491	12.5	247	12.6	0.83
Having health insurance	2646	67.2	1117	56.8	<0.0001
With ≥ 2 co-morbidities[e]	1642	41.7	693	35.2	<0.0001
Self-reported health status: excellent/good	749	19.0	384	19.5	0.65
History of hypertension	1184	30.1	527	26.8	0.01
History of diabetes mellitus	661	16.8	291	14.8	0.06
Self-reported vision status: excellent/good	1634	41.5	766	38.9	0.08
With any ocular disease	1376	34.9	669	34.0	0.45
Glaucoma diagnosed	162	4.3	88	4.5	0.74
Self-reported cataract history	388	9.9	169	8.6	0.14

	Analysis cohort[a] (N=3939)		Nonparticipants or Excluded[b] (N=1968)		
Characteristics	**n**	**%**	**n**	**%**	***P Value*[c]**
Self-reported glaucoma history	107	2.7	52	2.6	0.96
Self-reported macular degeneration history	29	0.7	13	0.7	0.88
Self-reported diabetic retinopathy history	82	2.1	37	1.9	0.95

SD= standard deviation.

[a] Participants completing the clinical examination at 4-year follow-up.

[b] Nonparticipants of the follow-up examination participated in the baseline examination but did not have glaucoma data at follow-up.

[c] Chi-square test for categorical variables; t test for continuous variables.

[d] Acculturation was measured using the short-form Cuellar Acculturation Scale.

[e] Comorbidities refer to the summation of the following medical conditions: arthritis, diabetes mellitus, back pain, hypertension, deafness, asthma, angina, skin cancers, heart disease, stroke, and heart failure.

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Table 2

Four-Year Incidence of Open-angle Glaucoma in participants in the Los Angeles Latino Eye Study (LALES)

	Incidence in the first eye				Incidence in the second eye				Incidence in either eye			
Age group	**n**	**N**	**%**	**(95%CI)**	**n**	**N**	**%**	**(95%CI)**	**n**	**N**	**%**	**(95%CI)**
40-49	15	1465	1.0	(0.5-1.5)	2	12	16.7	(0-37.8)	17	1477	1.2	(0.6-1.7)
50-59	17	1210	1.4	(0.7-2.1)	0	19	-	-	17	1229	1.4	(0.7-2.0)
60-69	31	757	4.1	(2.7-5.5)	5	32	15.6	(3.0-28.2)	36	789	4.6	(3.1-6.0)
70-79	17	293	5.8	(3.1-8.5)	2	23	8.7	(0-20.2)	19	316	6.0	(3.4-8.6)
80+	7	47	14.9	(4.7-25.1)	2	5	40.0	(0-82.9)	9	52	17.3	(7.0-27.6)
Crude overall	87	3772	2.3	(1.8-2.8)	11	91	12.1	(5.4-18.8)	98	3863	2.5	(2.0-3.0)
Age-standardized*			2.5	(1.9-3.0)			10.9	(4.5-17.4)			2.6	(2.1-3.2)

Note: The 167 participants with glaucoma at baseline are excluded from the analysis cohort

*Age-standardized incidence rates are adjusted for LALES population. n=number with incident open-angle glaucoma, N=number at risk

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Table 3

Four-Year Incidence of Ocular Hypertension in participants in the Los Angeles Latino Eye Study (LALES)

	Incidence in the first eye				Incidence in the second eye				Incidence in either eye			
Age group	**n**	**N**	**%**	**95% CI**	**n**	**N**		**95% CI**	**n**	**N**		**95% CI**
40-49	30	1419	2.1	1.4-2.9	3	15	20.0	0-40.2	33	1434	2.3	1.5-3.1
50-59	40	1145	3.5	2.4-4.6	6	31	19.4	5.5-33.3	46	1176	3.9	2.8-5.0
60-69	36	715	5.0	3.6-6.8	8	15	53.3	28.1-78.6	44	730	6.0	4.4-7.9
70-79	15	271	5.5	2.8-8.3	4	10	40.0	9.6-70.4	19	281	6.8	3.8-9.7
80+	3	39	7.7	0-16.1	3	6	50.0	10.0-90.0	6	45	13.3	3.4-23.3
Crude overall	124	3589	3.5	2.9-4.1	24	77	31.2	20.8-41.5	148	3666	4.0	3.4-4.7
Age-standardized*			3.6	2.3-4.2			29.0	17.4-40.6			4.2	3.5-4.9

*Age-standardized incidence rates are adjusted for LALES population. n=number with incident open-angle glaucoma, N=number at risk

Table 4

Completeness of Data for Glaucoma Classification for Participants with Incident Open-Angle Glaucoma in the Los Angeles Latino Eye Study

	Gradable Disc Photographs* [n(%)]	Clinical Disc Examination Data Only [n(%)]	No Disc Data [n(%)]	Total [n(%)]
≥2 visual fields†	49(50.0%)	4(4.1%)	1(1.0%)	54(55.1%)
1 visual field	31(31.6%)	6(6.1%)	2(2.0%)	39(39.8%)
No visual field	3(3.1%)	1(1.0%)	1(1.0%)	5(5.1%)
Total	83(84.7%)	11(11.2%)	4(4.1%)	98(100%)

*Simultaneous stereoscopic optic disc photographs.

†Humphrey C24 Swedish Interactive Threshold Algorithm Standard and/or full threshold C24-2.

Table 5

Frequency of Specific Diagnostic Criteria for Defining Open-Angle Glaucoma in Los Angeles Latino Eye Study Participants (n = 98)

Diagnostic Criteria	Frequency (n=98)	
	n	%
A. Evidence of visual field* and optic disc damage		
1. Open angle, ≥2 reliable, abnormal visual field tests with excellent congruence and optic disc damage both characteristic of glaucoma	16	16.3
2. Open angle, ≥1 abnormal visual field test(s) and optic disc damage both characteristic of or compatible with glaucoma	39	39.8
3. End-stage disease with visual acuity ≤20/200 and a cup–disc ratio of 1.0 and absence of visual field data	1	1.0
4. Combinations of visual field and optic disc abnormalities with fair congruence between fields that are both compatible with glaucoma	14	14.3
B. Evidence of either visual field* or optic disc damage		
5. ≥1 abnormal visual field test(s) that are characteristic of or compatible with glaucoma and no evidence of optic disc damage	9	9.2
6. Characteristic or compatible glaucomatous optic disc damage with no evidence of visual field abnormality	19	19.4

*Humphrey C24 Swedish Interactive Threshold Algorithm Standard and/or full threshold C24-2.

Table 6

Comparison of Clinical and Optic Disc Characteristics at Baseline and 4-year Follow-up Among Participants with Incident Open Angle Glaucoma in the Los Angeles Latino Eye Study

	Baseline	Follow-up	*P*-value
Clinical Characteristics			
Age(yrs)			
Mean±SD	62.8±11.6	67.1±11.6	
Median	64.0	68.0	
IOP(mmHg)*			
Mean±SD	16.5±5.1	16.2±5.2	0.82
Median	16.0	15.0	
%IOP>21 mmHg*	14(15.1)	14(15.1)	0.76
Mean defect(dB)			
Mean±SD	-5.2±7.2	-5.8±6.9	0.002
Median	-2.5	-3.3	
PSD(dB)			
Mean±SD	3.3±2.6	4.1±2.6	0.0006
Median	2.3	3.3	
CCT(μm)			
Mean±SD	547.3±43.5	547.1±44.3	0.84
Median	543.5	539	
Optic Disc Characteristics			
HCDR			
Mean±SD	0.5±0.1	0.6±0.1	<0.0001
Median	0.5	0.6	
VCDR			
Mean±SD	0.5±0.1	0.7±0.1	<0.0001
Median	0.5	0.7	
HCDR>0.7[n(%)]	1(1.1)	14(16.1)	0.002
VCDR>0.7[n(%)]	1(1.1)	32(36.8)	<0.0001
HCDR asymmetry of ≥0.3[n(%)]	0	10(11.5)	-
VCDR asymmetry of ≥0.3[n(%)]	0	16(18.4)	-
Disc/NFL hemorrhage [n(%)]	1(1.1)	2(2.3)	0.56
Peripapillary atrophy [n(%)]	54(62.1)	64(73.6)	0.09
Diffuse thinning of neural rim to disc margin [n(%)]	0	7(8.0)	-
Notching of neural rim [n(%)]	0	51(58.6)	-

OHT: ocular hypertension; IOP: intraocular pressure; PSD: pattern standard deviation; CCT: central corneal thickness

HCDR: horizontal cup-disc ratio; VCDR: vertical cup-disc ratio; NFL: nerve fiber layer

*Participants with treatment history of glaucoma are not included. This analysis was done on participants with first-eye incidence only.

Table 7

Comparison of Clinical and Optic Disc Characteristics at Baseline and 4-year Follow-up Among Participants with Incident Ocular Hypertension in the Los Angeles Latino Eye Study

	Baseline	Follow-up	*P*-value
Clinical Characteristics			
Age(yrs)			
Mean±SD	58.0±10.7	62.3±10.2	
Median	58.0	62.0	
IOP(mmHg)*			
Mean±SD	16.8±2.5	23.2±2.5	<0.0001
Median	16.7	22.3	
%IOP>21 mmHg	0	92(74.2%)*	-
Mean Defect(dB)			
Mean±SD	-2.6±4.9	-2.3±4.8	0.73
Median	-1.4	-1.0	
PSD(dB)			
Mean±SD	2.6±2.1	2.5±1.8	0.57
Median	1.9	1.8	
CCT(μm)			
Mean±SD	563.4±29.5	558.2±31.2	0.002
Median	561	558	
Optic Disc Characteristics			
HCDR			
Mean±SD	0.4±0.1	0.4±0.5	0.38
Median	0.3	0.3	
VCDR			
Mean±SD	0.3±0.1	0.3±0.1	0.73
Median	0.3	0.3	
HCDR>0.7[n(%)]	0	0	-
VCDR>0.7[n(%)]	0	0	-
HCDR asymmetry of ≥0.3[n(°%)]	0	0	-
VCDR asymmetry of ≥0.3[n(%)]	0	0	-
Disc/NFL hemorrhage [n(%)]	0	2(1.6)	-
Peripapillary atrophy [n(%)]	42(33.9)	75(60.5)	<0.0001
Diffuse thinning of neural rim to disc margin [n(%)]	0	0	-
Notching of neural rim [n(%)]	0	0	-

OHT: ocular hypertension; IOP: intraocular pressure; PSD: pattern standard deviation; CCT: central corneal thickness

HCDR: horizontal cup-disc ratio; VCDR: vertical cup-disc ratio; NFL: nerve fiber layer

*Participants with treatment history of glaucoma are not included. This analysis was done on participants with first-eye incidence only.

Table 8

Incidence of Open-Angle Glaucoma in Population based Studies

Study	Country	Year	Sample size	OAG cases	Years	Incidence Estimate	Average/year
Melbourne	Australia	2002	3271	12	5	1.1%/5years	0.22%
Rotterdam	Netherlands	2005	6780	87	6.5	1.8%/5years	0.36%
Barbados	West Indies	2001	3427	148	4	4.3%/4years	1.08%
Barbados	West Indies	2006	3222	266	9	9.4%/9years	1.04%
LALES	USA	2008	4435	87	4	2.45%/4years	0.61%

OAG: open angle glaucoma