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Risk Factors for Incident Cortical, Nuclear, Posterior Subcapsular, and Mixed Lens Opacities: The Los Angeles Latino Eye Study

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Abstract

Purpose—To identify socio-demographic and biological risk factors associated with the 4-year incidence of nuclear, cortical, posterior sub-capsular (PSC), and mixed lens opacities.

Design—Population-based, longitudinal study.

Participants—Four thousand six hundred fifty-eight Latinos 40 years and older from 6 census tracts in Los Angeles, California.

Methods—Participants underwent an interview and detailed eye examination, including best-corrected visual acuity and slit-lamp assessment of lens opacities using the Lens Opacities Classification System II at baseline and again 4 years later. Each opacity type was defined in persons with a LOCS II score of 2 or more. Univariate and forward stepwise logistic regression analyses were used to identify independent baseline risk factors associated with 4-year incidence of nuclear only, cortical only, PSC only, and mixed (when more than one opacity type developed in a person) lens opacities. These comprised 4 mutually exclusive groups, and were based on person rather than eye.

Main Outcome Measures—Odds ratios for independent risk factors associated with 4-year incidence of nuclear-only, cortical-only, PSC-only, and mixed lens opacities.

Results—Of the 3471 participants with gradable lenses in the same eye at baseline and 4-year follow-up, 200 (5.8%) had incident nuclear-only opacities, 151(4.1%) had incident cortical-only opacities, 16 (0.5%) had incident PSC-only lens opacities, and 88 (2.5%) had mixed lens opacities. Independent baseline risk factors for incident nuclear-only lens opacities included older age, current smoking, and presence of diabetes. Independent risk factors for incident cortical-only lens

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[3]A list of members of the Los Angeles Latino Eye Study Group is available at http://aaojournal.org (Appendix 1)

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This article contains online-only material. The following should appear online-only: Appendix 1

opacities included older age and having diabetes at baseline. Female gender was an independent risk factor for incident PSC-only lens opacities. Older age, and presence of diabetes at baseline exam were independent risk factors for incident mixed lens opacities. Specifically, in diabetics, higher levels of hemoglobin A1c was associated with greater risk for 4-year incident nuclear-only, cortical-only and mixed lens opacities.

Conclusions—Improved diabetic control and smoking prevention may reduce the risk of developing lens opacities. Understanding both modifiable and non-modifiable risk factors provides insight into the development of lens opacification.

Half of the world's blindness and half of the United States' visual impairment can be attributed to age-related cataracts.[1,2] While cataract surgery is generally quite safe and effective, it is not always without complications, and more significantly, it is very expensive. Treatment of age-related cataracts costs Medicare approximately 4.8 billion dollars per year, more than the combined costs of age-related macular degeneration (AMD), diabetic retinopathy, and glaucoma.[3] Furthermore, access to cataract surgery can represent a major barrier for patients, for financial, social, and logistical reasons, not only in the developing world but also in the United States.[4–6]

Understanding the biological risk factors behind lens opacity formation may inform research on the pathogenesis of lens opacity formation, as well as related early pharmacotherapeutic efforts to prevent or reduce progression of lens opacification. More importantly, however, it can aid current public health efforts to reduce the burden of modifiable risk factors. Studying these risk factors in Latinos is especially important because Latinos are the fastest-growing ethnicity in the United States and they are more likely than non-Hispanic whites and African Americans to have visual impairment.[7,8] The Los Angeles Latino Eye Study (LALES) is a population-based study that has examined the epidemiology of various eye diseases in a group of Latinos ages 40 and over living in Los Angeles County, California. The longitudinal data now available studying this population over a 4-year period provides a rich way to deduce possible causality between risk factors present at baseline and the subsequent incidence of various lens opacities. The current study's objective was to examine the relationship between sociodemographic and biological risk factors present at baseline and the 4-year incidence of nuclear, cortical, and posterior subcapsular (PSC) lens opacities in LALES participants.

Methods

Study Population

The LALES participants were self-identified Latinos living in La Puente, California, ages 40 years and older. The socioeconomic and demographic characteristics of Latinos in the 6 census tracts of La Puente are representative of Latinos of Mexican origin in Los Angeles County, California, and the United States. Additional details regarding the sampling strategy, study design, and baseline data are available in a previous publication.[9] The Los Angeles County, University of Southern California Medical Center Institutional Review Board Ethics Committee approved this study, and study procedures adhere to the Declaration of Helsinki. Written, informed consent was obtained from all participants. Baseline examinations were performed between 2000 and 2003, and 4-year follow-up exams were performed between 2004 and 2008. At baseline, 6357 of 7789 eligible participants (82%) completed an in-home questionnaire and ophthalmic examination. All eligible participants who completed the baseline LALES exam were invited to participate in the 4-year follow-up home interview and clinical examination, which were similar to those conducted at baseline. Trained technicians and ophthalmologists performed a comprehensive ocular examination using standardized protocols.

Examination Procedures and Lens Grading

Presenting visual acuity and best-corrected visual acuity were documented using the Early Treatment of Diabetic Retinopathy Study (ETDRS) protocol. Slit-lamp examination following maximal pupillary dilation with tropicamide 1% and phenylephrine 2.5% was used to assess the lens. The Lens Opacities Classification System II (LOCS II), which is based on photographic standards, was used to categorize opacities into 5 posterior subcapsular (P0, PI, PII, PIII, PIV), 5 nuclear (NO, NI, NII, NIII, NIV), and 7 cortical (C0, Ctr, CI, CII, CIII, CIV, CV) gradings of increasing severity. Phakic status (phakic, pseudophakic, or aphakic) was recorded for each eye. When lens assessment was not possible, reasons for not grading in one or both eyes were documented. The same 2 examiners performed lens grading at baseline and 4-year follow-up examinations; both were masked to previous examination results. The reproducibility of LOCS II grading was evaluated between the two examiners regularly throughout the study. They performed masked, replicate grading on 50 participants independently every 5–6 months, and their LOCS II gradings were measured for agreement using proportionally weighted kappa statistics. Results showed moderate to good intergrader agreement for each opacity type (nuclear opacities, weighted κ [95% confidence interval (CI)] = 0.76 [0.66–0.87]; cortical opacities, weighted κ = 0.67 [0.56–0.79]; and PSC opacities, weighted κ = 0.66 [0.24–1.0].

Definition of Incident Lens Opacities

Nuclear lens opacity was defined by LOCS II grading of NII, NIII, or NIV; cortical lens opacity was defined by LOCS II grading of CII, CIII, CIV, or CV; PSC lens opacity was defined by LOCS II grading of PII, PIII, or PIV. Incident lens opacities were defined as the development of nuclear-only, cortical-only, PSC-only, or mixed-type opacities (when more than one type developed) at 4-year follow-up in participants without any opacity in either eye at baseline. These comprised 4 mutually exclusive groups and were based on *person* rather than eye. For example, if a patient developed nuclear and cortical lens opacities in the same eye (each with LOCS II scores of 2 or more), this was considered a mixed-type lens opacity. Additionally, if a patient developed cortical-only lens opacity in one eye and a PSC-only lens opacity in the other eye, this was also considered a mixed-type lens opacity. Only participants with gradable LOCS II scores for all three opacity types were considered.

Risk Factor Assessment

Candidate socio-demographic and clinical factors for each lens opacity type were taken from baseline medical and family history in-home interview, as well as from clinical and ocular parameters measured during the baseline clinical examination. Parameters taken from the interview included age, gender, income level, educational level, birthplace, acculturation score (based on Cuellar's 5-point acculturation score, including preferred language and which language the person can speak, read, or write), current smoking history, former smoking history, self-reported history of hypertension, and family history of lens opacities. Those elicited from the clinical evaluation included hemoglobin A1c level, body mass index, diagnosis of glaucoma, presence of diabetes mellitus, intraocular pressure, spherical equivalent refractive error, presence of large drusen on dilated fundus exam, and diagnosis of AMD on grading of fundus photographs using the Wisconsin Age-Related Maculopathy Grading System. Body mass index was defined as weight in kilograms divided by the square of the height in meters (kg/m^2). Body mass index categories were grouped as underweight ($<18.5\ kg/m^2$), normal weight ($18.5–24.9\ kg/m^2$), overweight ($25.0–29.9\ kg/m^2$), and obese ($\geq 30.0\ kg/m^2$).

Statistical Analyses

Univariate associations of each socio-demographic and clinical characteristic with each of the four lens opacity types were determined using chi-square analyses and t-test procedures. Parameters with a *P*-value ≤ 0.2 were considered as candidate risk factors for the multivariable logistic regression model. Stepwise logistic regression procedures were conducted to evaluate the independent associations and order of importance for each characteristic. The generalized estimating equation was used to adjust for between-eye correlation for each person to assess any potential differences between per-eye versus per-participant analyses. In addition, local regression methods adjusting for other covariates in the multivariate logistic model were used to generate LOWESS (locally weighted smoothing regression) plots to characterize the nature of the relationships between some of the risk factors and the lens opacity types. Analyses were performed using the Statistical Analysis System (version 9.0, SAS Institute Inc, Cary, NC, and STATA Corp, College Station TX).

Results

Of the 6,357 participants examined at baseline, 6,100 were living and eligible for the 4-year follow-up examination. Of these, 4,658 participated in the 4-year follow-up examination, and 4139 had LOCS II gradable lens opacities in the same eye at baseline and 4-year follow-up. Mean age of participants was 51.72 (±8.34) years, and were more likely to be female and married. Detail Baseline characteristics of participants and non-participants in the follow-up study have been previously reported.[10]

Of the 4,139 LALES participants with gradable lens opacities both at baseline and follow-up, 3,471 participants had no lens opacities at baseline and constituted our at-risk cohort for developing lens opacities over 4 years. The other 668 had lens opacities present at baseline and were thus excluded. Of the 3,471 with no lens opacities at baseline, 200 (5.8%) had incident nuclear-only lens opacities, 141 (4.1%) had incident cortical-only lens opacities, 16 (0.5%) had incident PSC-only lens opacities, and 88 (2.5%) had incident mixed-type lens opacities. The remaining 3026 (87.2%) continued to have no lens opacities at 4-year follow-up.

Table 1 and 2 show the distribution of the socio-demographic and clinical characteristics at baseline stratified by lens opacity type. In general, participants with incidence of nuclear-only and mixed type were more likely to be older, and to have glaucoma than those with no opacity; a greater proportion of women had incident PSC-only, and Individuals with cortical, nuclear, and mixed type were more likely to have diabetes compared to those with no opacity.

Candidate risk factors significant at the univariate level with P-value ≤ 0.2 were included in the multivariate model. These included, age, gender, acculturation, education, income, presence of diabetes, systolic blood pressure, smoking status, hypertension, intraocular hypertension, glaucoma diagnosis, and presence of large drusen. In addition, we conducted a sub-analysis among diabetics to further explore the relationship of hemoglobin A1C and 4-year incidence of lens opacities. When hemoglobin A1C was entered in the model, the risk of 4-year incidence for lens opacities varied by level of hemoglobin A1C. Higher levels of hemoglobin A1C were associated with higher risk of developing lens opacities.

In the multivariate model, the independent risk factors associated with development of nuclear-only lens opacities at 4-year follow-up were older age (odds ratio (OR) 1.61; $P<0.0001$), report of current smoking at baseline interview (OR 1.72; $P=0.01$), and presence of diabetes mellitus (OR 1.11; $P=0.05$) (Table 3). For cortical-only lens opacities, the independent risk factors were older age (OR 1.08; $P<0.0001$) and presence of diabetes

mellitus (OR 2.32; $P<0.0001$) (Table 3). Female gender was independently associated with development of PSC-only lens opacities (OR 10.23; $P=0.02$), and independent risk factors for development of mixed-type lens opacities included older age (OR 1.15; $P<0.0001$), and presence of diabetes mellitus (OR 1.15; $P<0.0001$) at baseline, (Table 3). In addition, when we repeated our risk factor analyses on a per-eye basis rather than per-person basis, the results were similar, so we have focused here on per-person analyses.

A LOWESS plot was generated to predict incidence of nuclear and cortical lens opacities with older age at baseline, adjusting for other baseline covariates (Fig. 1). This showed that there was a stronger association between older age and incident nuclear lens opacities as compared to incident cortical opacities. While there is a relatively sharp rise in predicted incident nuclear opacities with every year of older age at baseline, the predicted incidence of cortical lens opacities more slowly rises with age between ages 40 and 60 but reaches a relative plateau after the age of 60. A LOWESS plot was also used to predict incidence of nuclear and cortical lens opacities with higher levels of hemoglobin A1c, adjusting for covariates (Fig. 2). This showed a similar rise in predicted incidence of each lens opacity type with higher baseline hemoglobin A1c.

Discussion

This particular study, the Los Angeles Latino Eye Study (LALES), identifies socio-demographic and biological risk factors present at the baseline evaluation, for the development of nuclear, cortical, PSC, and mixed lens opacities over a 4-year period. It provides important epidemiologic data in a unique segment of the United States population and, thus, may inform future targeted public health efforts in cataract prevention. In addition to becoming one of the largest and fastest growing segments of the United States population, Los Angeles Latinos are unique from a socioeconomic and acculturation standpoint. 86% had household income less than $40,000, 76% of study participants were born outside of the United States, and 67% had an acculturation score (as described under Methods) of ≤ 1.9.[9] Additionally, this group carries a high burden of diabetes; 17% of the study population reported a history of diabetes at baseline.[9] By collecting data longitudinally, the present study is able to conjecture a causal association between baseline clinical characteristics and the subsequent development of particular lens opacities. While we cannot yet compare the epidemiology of cataract among our Latino study population to other Los Angeles populations, we have previously reported that Los Angeles Latinos have a somewhat lower incidence of cortical lens opacities and somewhat higher incidence of nuclear opacities compared to the Afro-Carribean population from the Barbados Eye Study, a study with similar methodology to our own.[11,12]In this study, older age, higher hemoglobin A1c, current smoking, and female gender were independent baseline predictors of various incident lens opacities among Los Angeles Latinos. These findings are supported by other population-based eye studies.

AGE

Older age at baseline was found to be a risk factor for the development of nuclear, cortical, and mixed lens opacities in this longitudinal LALES investigation. The link between older age and cataract has been well reported. For example, both the Barbados Eye Study and the Age-Related Eye Disease Study found age to be a significant risk factor for incident nuclear, cortical, and PSC lens opacities.[13–15] Nuclear cataracts occur as the result of changes to crystallins in the lens nucleus, and oxidation of proteins is thought to play an especially important role in this process.[16–20] Some of these lens nucleus changes have been linked to aging and are thought to contribute to hardening of the lens even before cataract formation.[17,21] The strong epidemiologic link between older age and nuclear cataract formation shown in our and previous investigations[13,15, 22] may be the result of these age-

related changes of progressive hardening and then opacification of the lens nucleus. It is possible that the cumulative exposure to such oxidative factors with older age may promote these lens protein changes and thus play a role in nuclear lens opacity formation with older age. In contrast to the observations that some degree of nuclear sclerosis occurs in nearly everyone of older age, older individuals do not routinely develop evidence of cortical opacity. This opacity type begins with cellular disruption of cortical fiber cells near the equator of the lens and progresses in severity if an increasing amount of adjacent lens fiber cells become involved in the damage.[23,24] Our study showed that the risk for cortical lens opacities with older age is less than the risk for nuclear opacities with higher age; it also appears to be more important between the ages of 40 and 60, becoming less important with higher age beyond 60 (Fig. 1). While the link between age and cortical opacity has been previously reported[14,15], the observation that age may be more important in the cortical opacity development among a younger subset has not been made in other studies. This observation suggests that factors other than age may be more important in predicting development of cortical opacities, and it supports the idea that cumulative exposure to oxidation with older age may play a relatively *more* important role in the development of nuclear opacities. More research is necessary to verify these preliminary observations.

DIABETES

Higher hemoglobin A1c, a biological marker for uncontrolled diabetes, was also independently associated with the 4-year incidence of nuclear, cortical, and mixed lens opacities in our study. The relationship of diabetes and poor diabetic control with incidence of various lens opacities has been well documented in other large epidemiologic studies, including the Barbados Eye Study, Beaver Dam Eye Study, Pathologies Oculaires Liées à l'Age (POLA) Study, and the Age-Related Eye Disease Study (AREDS).[15,25–27] Significant research efforts have explored the pathogenesis of diabetic cataracts and have emphasized the role of the polyol pathway, whereby aldose reductase catalyzes the reduction of glucose to sorbitol, in the initiation of diabetic lens changes.[28] This leads to an osmotic intracellular accumulation of fluid in lens fibers and can result in rapid formation of cortical lens opacities in the setting of uncontrolled hyperglycemia, as is often observed in young diabetic patients.[28] Additionally, increased glucose levels in the aqueous are thought to cause glycation of lens proteins, leading to increased levels of free radicals[29,30]. The glycation is then worsened by the impaired ability of the diabetic lens to handle oxidative stress.[30,31] This increased oxidative stress may lead to the subsequent formation of nuclear and mixed-type cataracts. This theoretical chronology of events may be supported by the fact that in LALES, cortical opacities often developed first and at an earlier age and later progressed to become a mixed lens opacity.[12]

Interestingly, animal studies initially suggested the potential utility of aldose-reductase inhibitors and antioxidants in the prevention of diabetic cataracts,[32–34] but subsequent human studies have shown that such antioxidant supplementation may have minimal, if any, effect in preventing lens opacities.[35,36] For this reason, and given that 8.5% of Americans and 11.8 % of United States Latinos live with diabetes,[37] public health efforts to promote improved diabetic control may significantly reduce the burden of cataract-related visual impairment and eye care, both in the United States and around the world.

SMOKING

Our study demonstrated that smoking is an independent risk factor for the development of nuclear-only lens opacities. This relationship has been well demonstrated by the Blue Mountains Eye Study, the Beaver Dam Eye Study, and the Longitudinal Study of Cataract.[22,38,39] Even exposure to indoor cooking smoke has been linked to nuclear cataract.[40] A dose-response relationship between the amount of smoking exposure and the

risk for nuclear lens opacities has also been well documented.[38,41–43] In contrast, AREDS most recently reported that smoking was associated with incident cortical lens opacities and cataract surgery, but no association was reported with nuclear opacities.[15] Mechanisms behind smoking as a potential etiologic agent for nuclear sclerosis most likely involve oxidative damage of the lens. This is supported by the findings of reduced antioxidant levels in smokers; increased reactive advanced glycation end products in smokers, both in the lenses and systemically; and of the direct toxicity of heavy metals from cigarette smoke to the lens.[44–49] Some basic science studies have suggested a particularly important role for oxidative damage in nuclear opacity development,[16–17,50] and this is supported by the epidemiologic data demonstrating the specific relationship between smoking and nuclear opacity development. In any case, these epidemiologic findings necessitate a push toward smoking prevention and cessation in an effort to reduce the development of nuclear lens opacities.

FEMALE GENDER

Female gender was the only risk factor found to be associated with the 4-year incidence of PSC lens opacities. Previously, we showed that female gender was an independent risk factor for prevalent mixed-type lens opacities.[51] The Barbados Eye Study suggested that female gender increased the risk for incident nuclear and cortical lens opacities; and the POLA study demonstrated an association between female gender and prevalent cortical lens opacities and having obtained cataract surgery.[13,14,27] Most recently, AREDS reported an increased risk of cortical cataract in females but a decreased risk of PSC, which counters our findings.[15] In our collected demographic and clinical variables, there were no underlying differences between males and females to explain the relationship between female gender and development of PSC opacities. This association may be related to differing genetic or environmental factors in the LALES population, or alternatively, it may represent an artifact of the small number of participants with the studied outcome (only 16 participants developed PSC opacities in the 4-year study period).

This population-based, longitudinal study of Los Angeles Latinos over a 4-year period greatly enhances our understanding of baseline predictors for the development of nuclear, cortical, PSC, and mixed lens opacities. It has allowed us to demonstrate the temporal relationship of risk factors predisposing to subsequent development of various lens opacities in this study population. And perhaps it has suggested important negative findings in identifying risk factors for lens opacity development. For example, myopia has been suggested in several cross-sectional epidemiology studies, including our own, to be associated with the presence of nuclear lens opacities.[13,51] The absence of this relationship in our longitudinal study, as well as the lack of association with axial length, suggests that the previously described relationship may be entirely related to the myopia induced by nuclear sclerosis rather than any causal effect of pre-existing myopia on the development of nuclear sclerosis. A major limitation of the current investigation is the smaller sample sizes of participants who developed a particular outcome, especially since particular lens opacity outcomes were defined by having developed that lens opacity type alone in the 4-year period. This may explain why there was only one significant risk factor found for incident PSC lens opacities. For example, while oral steroid use (based on patient recall) was assessed in a subsample of the entire cohort, it did not reveal an association between oral steroid use and PSC opacities. This likely represents the limited power to assess relationships with PSC due to our limited number of incident PSC only opacities in our population. Additionally, because of our limited sample sizes for the group with incident mixed opacities, we were unable to distinguish in our risk factor analyses between participants with mixed opacities within the same eye versus multiple opacities between both eyes. Overall, this study has demonstrated the importance of modifiable risk factors

such as diabetic control and smoking in subsequent incidence of lens opacities, and it has highlighted the importance of several other risk factors such as age, and female gender in the development of lens opacities. We hope that this data can guide public health efforts, especially among Los Angeles Latinos, to reduce the risk of cataract formation when possible and that it may guide future research efforts on the pathophysiology of various lens opacities.

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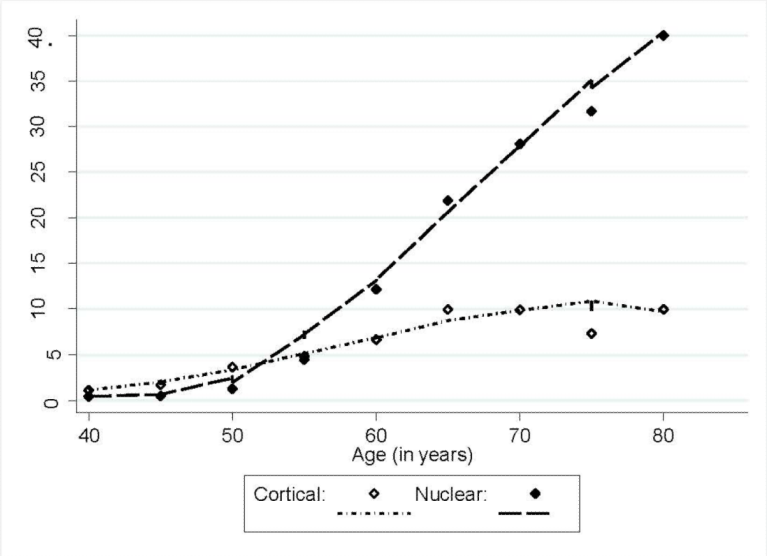

Figure 1.
LOWESS (locally weighted scatterplot smoothing regression) plots, which adjust for covariates, demonstrate a strong rise in predicted 4-year incidence of nuclear lens opacities with older age. With the case of cortical lens opacities, there is a smaller increase in incidence with age at baseline between the approximate ages of 40–60, but this relationship reaches a relative plateau beyond the age of 60.

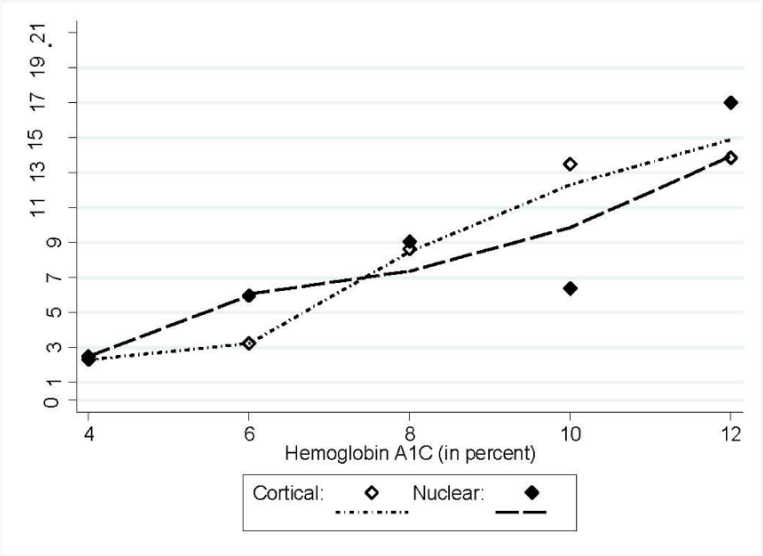

Figure 2.
LOWESS (locally weighted scatterplot smoothing regression) plots demonstrate a similar rise in predicted 4-year incidence of nuclear and cortical lens opacities with higher levels of hemoglobin A1c at baseline, adjusting for covariates.

Table 1

Distribution of Socio-demographic Characteristics Stratified by Lens Opacity Type in the Los Angeles Latino Eye Study Participants

Baseline Characteristics	No Opacity n=3026	Mixed Type n=88	Nuclear Only n=200	Cortical Only n=141	Posterior Subcapsular Only n=16
Mean Age (±SD)	50.41(7.5)	62.85(8.0)**	62.70(7.5)**	57.18(8.2)**	53.43(9.3)
Female Gender[†]	1788(59.1)	52(59.1)	118(59.0)	89(63.1)	15(93.8)**
Income <20,000	1178(44.0)	44(59.5)*	68(41.2)*	63(50.8)	4(28.6)
Low Acculturation Score <1.9[+]	2067(68.4)	53(60.2)	117(58.5)*	94(66.7)	11(68.8)
Less than High School Graduate	1890(62.6)	55(62.5)	138(69.0)*	105(74.5)*	9(56.3)

[†]Data is shown in column frequencies and percent (%) or mean and standard deviation (SD).

[+]Low acculturation score was defined as <1.9, using the Cuellar 9-item, 5-point scale developed for Mexican Americans and based on preferred language and which language the person can speak, read, or write. Each opacity type is compared to the no opacity group using a t-test for continuous variables and a chi-square test for categorical variables. Differences that are statistically significant at $p \leq 0.2$ are denoted with one asterisk(*), and at ≤ 0.05 are denoted with two asterisks(**). For example the mean age 62.8 (±8.0) for mixed type is significantly higher compared to the mean age (50.4±7.5) of the no opacity group, with p-value < 0.05. Risk factors with p-value ≤ 0.2 were considered as candidate risk factors for the multivariable logistic regression model.

Table 2

Distribution of Clinical Characteristics stratified by Lens Opacity Type in the Los Angeles Latino Eye Study Participants

Baseline Characteristics	No Opacity n=3026	Mixed Type n=88	Nuclear Only n=200	Cortical Only n=141	Posterior Subcapsular Only n=16
Current Smoker	404(13.4)	10(11.4)	32(16.0)*	21(14.9)	1(6.3)
Former smoker	708(23.5)	24(27.3)	56(28.1)	40(28.4)	4(25.0)
Diabetes Mellitus	511(16.9)	48(54.6)**	61(30.5)**	58(41.1)**	2(12.5)*
Hb A1C[‡] (mean±SD)	5.81(1.3)	7.26(2.1)**	6.27(1.7)*	6.88(2.2)**	6.02(1.9)
Hb A1C (>8%)	217(7.2)	25(28.4)**	24(12.0)*	35(24.8)**	2(12.5)
Hb A1C(>10%)	91(3.0)	13(14.8)	8(4.0)	21(14.9)*	2(12.5)
Hypertension	150(5.0)	7(7.8)	9(.5)	14(9.9)*	1(6.3)
Body Mass Index[+]					
Normal (reference)	303(10.10	8(9.2)	23(11.7)	13(9.3)*	2(12.5)
Overweight	1165(40.0)	30(34.5)	71(36.2)	55(39.3)	6(37.5)
Obese	1523(50.9)	49(56.3)	102(52.0)	72(51.4)	8(50.0)
Glaucoma	62(2.1)	6(6.8)**	16(8.0)**	4(2.8)*	1(6.3)*
Intraocular Pressure	14.24(3.0)	15.41(4.5)	15.13(3.2)*	14.58(2.9)	14.85(3.1)
Spherical Equivalent (Mean ±SD)	0.04(1.5)	0.38(3.0)	0.95(1.9)	0.35(1.9)	−0.30(3.6)
Family History Cataract	882(30.1)	23(27.7)	66(34.7)	52(38.5)*	6(42.7)
Large Drusen	348(11.7)	22(26.2)**	30(15.4)	14(10.0)	2(12.5)
Any AMD[≠]	238(7.9)	10(11.5)	23(11.7)	12(8.5)	0(0.0)

[†] Data is shown in column frequencies and percents (%) or mean and standard deviation (SD).

[‡] Hemoglobin A1C level

[+] Body Mass Index groups were divided into Normal (18.5–24.9 kg/m^2), Overweight (25.0–29.9 kg/m^2), and Obese (≥ 30.0 kg/m^2).

[≠] AMD: Age-related macular degeneration. The normal group comprised the reference group. Each opacity type is compared to the no opacity group using a t-test for continuous variables and a chi-square test for categorical variables. Differences that are statistically significant at $p \leq 0.2$ are denoted with one asterisk(*), and at ≤ 0.05 are denoted with two asterisks(**). For example, diabetes (41.1%) was significantly associated with cortical lens changes compare to those with no opacity (16.9%), with p-value < 0.05. Risk factors with a p-value ≤ 0.2 were considered as candidate risk factors for the multivariable logistic regression model.

Table 3

Independent Risk Factors for 4-year Incidence of Nuclear, Cortical, Posterior Subcapsular, and Mixed-type Lens Opacities in the Los Angeles Latino Eye Study

Nuclear-Only Lens Opacities

Independent Risk Factors[+]	OR (95% CI)[*]	*P*-Value
Age (per year)	1.61(1.14,1.19)	<0.0001
Current Smoking	1.72 (1.12,2.64)	0.01
Diabetes Mellitus	1.11 (1.01,1.22)	0.05

Cortical-Only Lens Opacities

Independent Risk Factors	OR (95% CI)	*P*-Value
Age (per year)	1.08 (1.05,1.10)	<0.0001
Diabetes Mellitus	2.32 (1.58,3.41)	<0.0001

Posterior Subcapsular-Only Lens Opacities

Independent Risk Factor	OR (95% CI)	*P*-Value
Female Gender	10.23 (1.35,77.57)	0.02

Mixed Lens Opacities

Independent Risk Factors	OR (95% CI)	*P*-Value
Age (per year)	1.15 (1.11,1.19)	<0.0001
Diabetes Mellitus	4.73 (2.86,7.82)	<0.0001

[*] Odds ratio (95% confidence interval); OR=odds ratio

[+] Candidate risk factors with p-Value < 0.2 at the univariate level were entered in the multivariate model. These include: age, gender, income, acculturation, education, diabetes, hemoglobin A1c, systolic blood pressure, smoking status, hypertension, intraocular pressure, glaucoma, and large drusen.