

Crystalline Lens Power and Refractive Error

Rafael Iribarren,¹ Ian G. Morgan,² Vinay Nangia,³ and Jost B. Jonas⁴

PURPOSE. To study the relationships between the refractive power of the crystalline lens, overall refractive error of the eye, and degree of nuclear cataract.

METHODS. All phakic participants of the population-based Central India Eye and Medical Study with an age of 50+ years were included. Calculation of the refractive lens power was based on distance noncycloplegic refractive error, corneal refractive power, anterior chamber depth, lens thickness, and axial length according to Bennett's formula.

RESULTS. The study included 1885 subjects. Mean refractive lens power was 25.5 ± 3.0 D (range, 13.9–36.6). After adjustment for age and sex, the standardized correlation coefficients (β) of the association with the ocular refractive error were highest for crystalline lens power ($\beta = -0.41$; $P < 0.001$) and nuclear lens opacity grade ($\beta = -0.42$; $P < 0.001$), followed by axial length ($\beta = -0.35$; $P < 0.001$). They were lowest for corneal refractive power ($\beta = -0.08$; $P = 0.001$) and anterior chamber depth ($\beta = -0.05$; $P = 0.04$). In multivariate analysis, refractive error was significantly ($P < 0.001$) associated with shorter axial length ($\beta = -1.26$), lower refractive lens power ($\beta = -0.95$), lower corneal refractive power ($\beta = -0.76$), higher lens thickness ($\beta = 0.30$), deeper anterior chamber ($\beta = 0.28$), and less marked nuclear lens opacity ($\beta = -0.05$). Lens thickness was significantly lower in eyes with greater nuclear opacity.

CONCLUSIONS. Variations in refractive error in adults aged 50+ years were mostly influenced by variations in axial length and in crystalline lens refractive power, followed by variations in corneal refractive power, and, to a minor degree, by variations in lens thickness and anterior chamber depth. (*Invest Ophthalmol Vis Sci.* 2012;53:543–550) DOI:10.1167/iovs.11-8523

The crystalline lens is a complex structure that grows throughout life.^{1,2} In children, the refractive power of the lens decreases with age.^{3–5} At the end of childhood, the crystalline lens refractive power is higher in hyperopic eyes than in myopic eyes,³ so that it correlates positively with the ocular refractive error and negatively with axial length. In adulthood,

a hyperopic shift in the ocular refractive error occurs, probably due to a reduction in crystalline lens refractive power.⁶ Later in life, when cataract develops, a myopic shift in ocular refractive error is found, potentially due to an increase in the crystalline lens refractive power. Although these changes in crystalline lens power throughout life have an impact on the refractive status of the eye, they have not been thoroughly studied yet, because of the difficulty in measuring the crystalline lens refractive power. The other components of ocular refraction (corneal refractive power, anterior chamber depth and axial length) are fairly easy to measure clinically, and their contributions to the refraction of the eye have intensively been studied.^{7–10} The refractive power of the lens can be measured precisely only *in vitro*,² but for clinical research, it can be estimated *in vivo* using Bennett's formula, if the distance refractive error and other ocular biometric parameters are available.¹¹ Bennett's formula has the advantage that it was developed to assess the refractive power of the natural lens at its location in the eye, in contrast with other formulas that were derived to calculate the refractive power of thin ideal lenses, such as implantable intraocular lenses. The accuracy of Bennett's formula depends on the validity of measurements of the biometric parameters that are included in the formula.

The hyperopic shift in ocular refractive error occurring in adulthood while the lens is increasing in thickness and curvature is known as the lens paradox.^{12,13} A lens with a steeper curvature would have been assumed to have a higher refractive power, whereas the hyperopic shift in refractive error of the eye implies a reduction in refractive lens power. The Reykjavik Eye Study was the first population-based study to report a negative correlation between crystalline lens power and refractive error of the eye, in addition to a negative correlation between the crystalline lens power and axial length in older subjects.¹⁰ The findings obtained for the older subjects differed from results in children. The finding of a negative correlation between crystalline lens refractive power on one side and ocular refractive error and axial length on the other side generated a paradox, if one took into account that ocular refractive error and axial length correlated negatively. That issue was recently examined in the Los Angeles Latino Eye Study (LALES) (Iribarren G, et al. *IOVS* 2010;51:ARVO E-Abstract 1717). A slight but statistically nonsignificant and negative correlation was found between the ocular refractive error and the crystalline lens refractive power, in addition to a negative correlation between crystalline lens refractive power and axial length. The LALES analysis in which subjects with cataract were excluded showed a hyperopic shift in the ocular refractive error with increasing age, parallel to a decrease in the crystalline lens refractive power in older hyperopic subjects. It was the opposite of what was described for children and young adults. In view of the incompleteness in the knowledge of the role of the refractive power of the crystalline lens, we performed the present analysis of data obtained in the Central India Eye and Medical Study with a relatively high prevalence of cataract to investigate the relationships between refractive power of the crystalline lens, overall refractive error of the eye, and degree of nuclear cataract.

From the ¹Department of Ophthalmology, San Luis Medical Center, Buenos Aires, Argentina; the ²Research School of Biology, College of Medicine, Biology and Environment, Australian National University, Canberra, Australia; the ³Suraj Eye Institute, Nagpur, Maharashtra, India; and the ⁴Department of Ophthalmology, Medical Faculty Mannheim of the Ruprecht-Karls-University Heidelberg, Mannheim, Germany.

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Corresponding author: Jost B. Jonas, Universitäts-Augenklinik, Theodor-Kutzer Ufer 1-3, 68167 Mannheim, Germany; jost.jonas@umm.de.

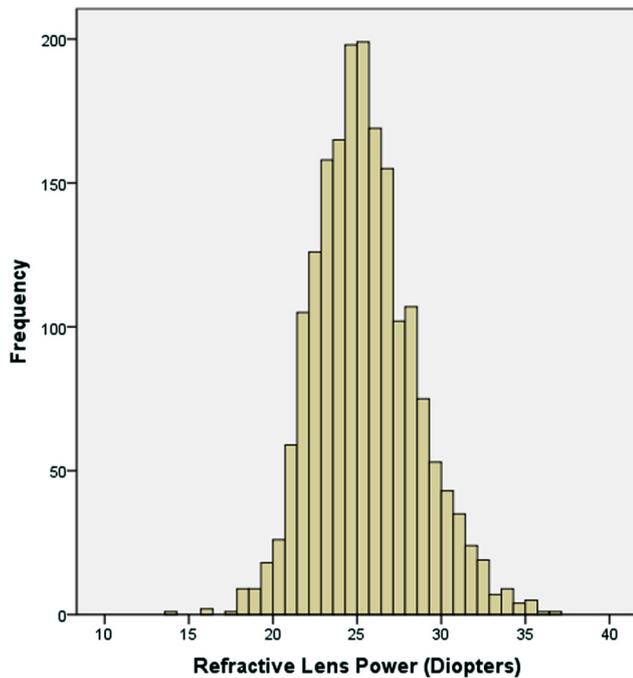


FIGURE 1. The distribution of refractive power of the lens in participants in the Central India Eye and Medical Study with an age of 50+ years.

METHODS

The Central India Eye and Medical Study is a population-based study performed in a rural region in Central India.^{14,15} It was performed in eight villages in the rural region of Central Maharashtra, approximately 40 km from Nagpur. The Medical Ethics Committee of the Medical Faculty Mannheim of the Ruprecht-Karls-University Heidelberg and the ethics committee of Suraj Eye Institute/Nagpur approved the study, and all participants gave informed consent, according to the Declaration of Helsinki. Inclusion criterion was an age of 30+ years. The villages were chosen for the study since they were located in a typically rural region of Central India at a relatively large distance to the next city (Nagpur). The Suraj Eye Institute was already known to the villagers, and the villagers had attended the institute for cataract surgery for the past 10 years. In a first step, social workers mapped the villages and went from house to house to list all inhabitants. They invited all villagers with an age of 30+ years to participate in the study including a bus ride to the hospital, a 1-day-long examination, meals, and a return bus ride to the village in the evening, all at no cost. Up to 20 subjects were examined per day. If cataract was diagnosed, cataract and intraocular lens implant surgery was offered free of charge to the patients. The recruitment of the study participants took place between 2006 and 2009.

Out of a total population of 13,606 villagers, 5885 subjects fulfilled the inclusion criterion of an age of 30+ years and were eligible for the

study. Of these 5885 subjects, 4711 (2520 [53.5%] women) participated, resulting in a response rate of 80.1%. Among the 1174 nonparticipants were 489 (41.7%) women; the mean age was 48.6 ± 14.1 years (median, 45; range, 30–95). The group of study participants and the group of nonparticipants did not differ significantly in age ($P = 0.06$), whereas the proportion of men was significantly ($P < 0.001$) higher in the group of nonparticipants. In the study population, mean age was 49.5 ± 13.4 years (median, 47; range, 30–100). The mean reported monthly income was $1,584 \pm 1,233$ Rupees (median, 1350; range, 200–15,000; 1 US\$ = ~50 Rupees). Of the 4711 subjects, 1623 (34.5%) subjects reported being illiterate, 1310 (27.8%) had attended school up to the 5th standard, 533 (11.3%) subjects attended the 6th to 8th standards, 1070 (22.7%) subjects attended the 9th to 12th standards, and 165 (3.5%) subjects received a higher level of education, such as graduate or higher. Ten (0.2%) subjects did not describe their level of education. Of the total 4711 subjects, 2206 (46.9%) indicated that they did not have a toilet facility, 62 (1.3%) used a public or shared a pit toilet, 557 (11.8%) used a public or shared a flush toilet or had their own pit toilet, and 1853 (39.3%) had their own flush toilet. Thirty-three subjects made no statements.

The participants underwent a detailed ophthalmic and medical examination, including standardized questions on socioeconomic background and lifestyle. Automated refractometry without cycloplegia and subjective refraction were performed for all subjects. Keratometry was performed with a nonautomatic keratometer (Appassawamy Association, Chennai, India). Sonographic ocular biometry was performed with an A-scan pachymeter (PacScan 300AP; Sonomed, Lake Success, NY). The pupil was dilated with tropicamide and phenylephrine 5% three times at 15-minute intervals, to attain the maximum pupillary dilatation. Digital photographs of the lens were taken and graded for nuclear sclerosis according to the Age-Related Eye Disease Study criteria (AREDS).¹⁶

The present study was focused on calculation of the refractive power of the lens and the relationship between crystalline lens power and other components of the optical system of the eye. Inclusion criteria for our study were the availability of full data on refractive error, ocular biometry, and lens-grading measurements. The exclusion criterion was any surgery on the lens (i.e., pseudophakic or aphakic eyes) or retina and missing data of refraction or biometry, which made lens power calculation impossible. As the calculation of refractive lens power included noncycloplegic distance refractive error, and since accommodation influences refraction in younger adults,^{17,18} only subjects with an age of 50 or more years were included in the analysis. The rate of participation for the eligible population with an age of 50+ years ($n = 2745$) was 2217 (80.8%) of 2745.

Statistical analysis was performed using a commercially available statistical software package (SPSS for Windows ver. 19.0; SPSS, Inc., Chicago, IL). The spherical equivalent was calculated as spherical value plus half the cylindrical value. Corneal power was calculated based on the radius of corneal curvature, assuming a refractive index of the cornea of 1.3315, as proposed by Olsen.¹⁹ The calculation of the refractive power of the lens was based on distance noncycloplegic refractive error, corneal refractive power, anterior chamber depth, lens thickness, and axial length according to the formula proposed by

TABLE 1. Participants of the Central India Eye and Medical Study Stratified by the Amount of Nuclear Cataract

	Nuclear Opacity Grades						
	1	2	3	4	5	6	7
<i>n</i>	0	2	33	418	791	471	170
Percentage of subjects	0.0	0.1	1.8	22.2	42.0	25.0	9.0
% Prevalence of myopia < -0.50 D*	0.0	0.0	9.1 ± 5.1 (0.0, 19.4)	7.4 ± 1.3 (4.9, 9.9)	15.6 ± 1.3 (13.0, 18.1)	57.5 ± 2.3 (53.1, 62.0)	54.1 ± 3.8 (46.6, 61.7)

* Mean ± SE (95% CI).

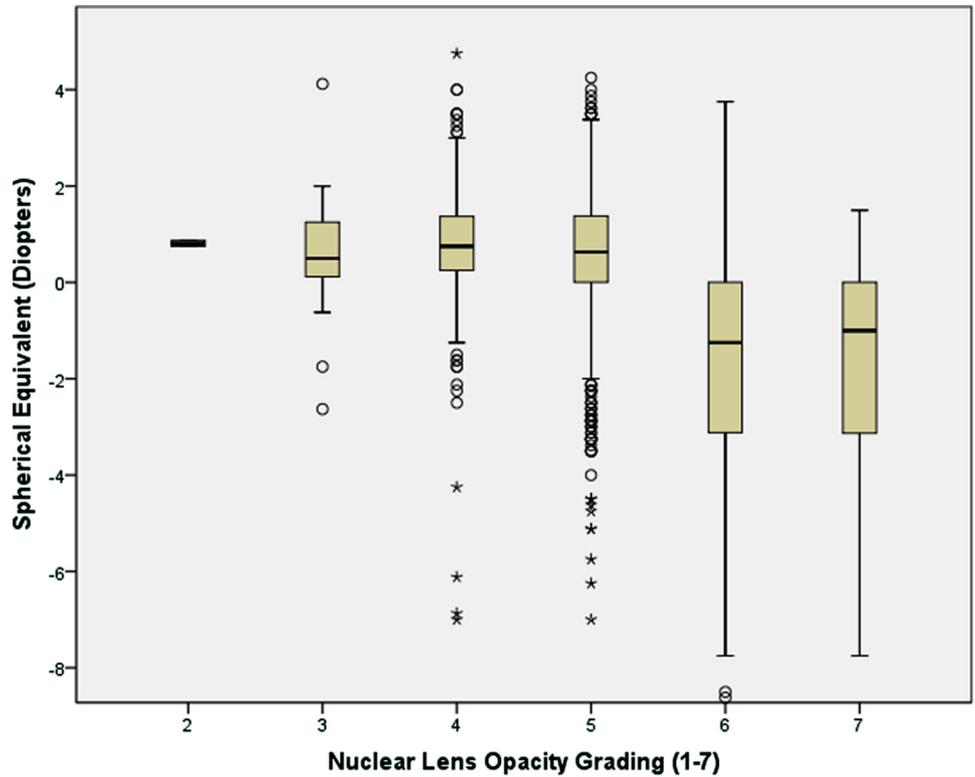


FIGURE 2. The distribution of refractive error (spherical equivalent) in participants in the Central India Eye and Medical Study stratified by the amount of nuclear lens opacity.

Bennett.⁷ The *A* and *B* constants in this formula were calculated using Gullstrand's reduced eye model.^{11,20} The study population was divided into eyes with grades 6 and 7 of the AREDS nuclear cataract assessment scheme, representing a considerable nuclear cataract, and into eyes with less marked nuclear cataract or no cataract at all (nuclear cataract grading ≤ 5). Myopia was defined as a refractive error (spherical equivalent) of less than -0.50 D, and hyperopia was defined as a refractive error (spherical equivalent) of more than $+1$ D. The remaining eyes were considered to be emmetropic. In a first step of the statistical analysis, the mean (\pm SD) values of spherical equivalent and refractive lens power were calculated across refractive groups and nuclear opacity groups by one-way analysis of variance (ANOVA) with post hoc Scheffé tests. In a second step, the associations between lens refractive power, ocular refractive error, and amount of nuclear lens opacity on one side and ocular biometric parameters on the other side were examined before and after adjustment for age and sex. In a third step of the statistical analysis, multivariate analyses were performed, including those parameters as independent parameters which showed a $P < 0.10$ in their univariate associations with the dependent parameter. Only right eyes were included in the analysis. Before, we had assessed that axial length, anterior chamber depth, lens thickness, and refractive error of the right eye were significantly associated with axial length ($P < 0.001$; correlation coefficient $r = 0.78$), anterior chamber depth ($P < 0.001$; $r = 0.66$), lens thickness ($P < 0.001$; $r = 0.48$), and refractive error ($P < 0.001$; $r = 0.72$), respectively, of the left eye. All P values were two-sided and were considered statistically significant when the values were < 0.05 .

RESULTS

The study included 1885 (914 [48.5%] male) subjects. The mean refractive power of the lens was 25.5 ± 3.0 D (mean, 25.2; range, 13.9–36.6) with a normal distribution (Fig. 1). Among the study population, 641 (34.0%) subjects had a nuclear cataract of grade 6 or 7 (Table 1). The prevalence of myopia and hyperopia changed significantly, depending on the lens opacity grading (Table 1). Subjects with mild lens opacity

had a greater prevalence of hyperopia, and subjects with a more marked lens opacity had a greater prevalence of myopia. The mean refractive error was more myopic for the high-opacity groups (Fig. 2).

In univariate analysis, crystalline lens power was significantly associated with higher age ($P < 0.001$), greater lens thickness ($P < 0.001$), shorter axial length ($P < 0.001$; Fig. 3), lower (i.e., more myopic) refractive error ($P < 0.001$), and more marked nuclear lens opacity ($P < 0.001$; Table 2). It was not significantly associated with sex ($P = 0.60$), corneal refractive power ($P = 0.76$), and anterior chamber depth ($P = 0.31$).

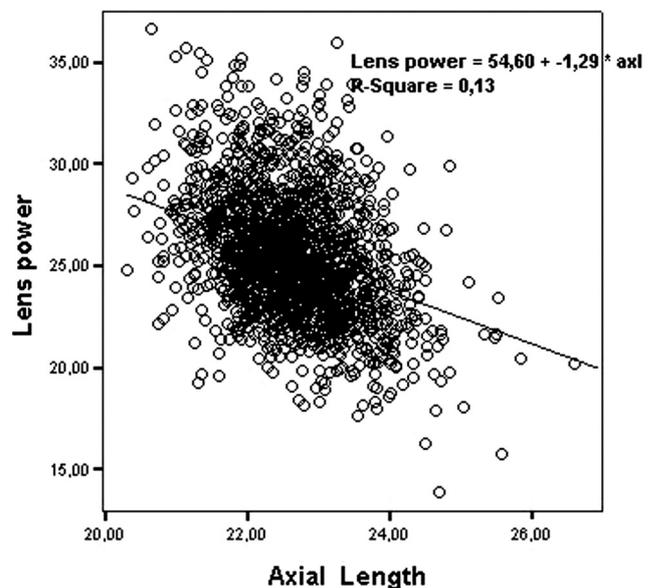


FIGURE 3. The correlation between crystalline lens power and axial length in participants in the Central India Eye and Medical Study.

TABLE 2. Correlation of the Refractive Power of the Lens with Ocular Biometric Parameters in Participants of the Central India Eye and Medical Study, Aged 50+ Years, Adjusted for Age and Sex (Univariate Analysis)

Parameter	<i>P</i>	Standardized Correlation	Nonstandardized Regression Coefficient β	95% CI for B Coefficient β
Lens thickness	<0.001	0.21	1.06	0.83 to 1.28
Axial length	<0.001	-0.42	-1.47	-1.63 to -1.31
Refractive error	<0.001	-0.45	-0.61	-0.67 to -0.56
Nuclear lens opacity	<0.001	0.27	0.86	0.69 to 1.03
Corneal refractive power	0.62	-0.01	-0.02	-0.11 to 0.06
Anterior chamber depth	0.17	0.03	0.29	-0.12 to 0.70

Similar results were obtained when the correlations were adjusted for age and sex (Table 2).

Refractive error of the eye was significantly associated with lower age ($P < 0.001$), the female sex ($P < 0.001$), higher central corneal thickness ($P < 0.001$), lower anterior chamber depth ($P = 0.01$), shorter axial length ($P < 0.001$), lower refractive lens power ($P < 0.001$), and more marked nuclear lens opacity ($P < 0.001$; Table 3). The standardized correlation coefficients were highest for refractive lens power and nuclear lens opacity grade, followed by axial length (Table 3). They were lowest for corneal refractive power and anterior chamber depth. Refractive error was not significantly associated with corneal refractive power ($P = 0.07$) and lens thickness ($P = 0.11$). Similar results were obtained if the correlations were adjusted for age and sex (Table 3).

Nuclear lens opacity grading was significantly associated with higher age ($P < 0.001$), lower (i.e., more myopic) refractive error ($P < 0.001$), lower central corneal thickness ($P < 0.001$), lower lens thickness ($P = 0.003$), longer axial length ($P < 0.001$), and higher crystalline lens power ($P < 0.001$). It was not significantly associated with the sex of the subject ($P = 0.37$), corneal refractive power ($P = 0.50$) and anterior chamber depth ($P = 0.57$; Table 4). Similar results were obtained if the correlations were adjusted for age and sex (Table 4).

In multivariate analysis, with lens refractive power as the dependent variable and age and sex, lens thickness, axial length, refractive error, and nuclear lens opacity grade as independent variables, lens refractive power was significantly associated with higher lens thickness ($P < 0.001$), shorter axial length ($P < 0.001$), lower (i.e., more myopic), refractive error ($P < 0.001$), and higher nuclear lens opacity grade ($P = 0.007$; Table 5).

In a similar multivariate analysis, with refractive error as the dependent variable and age, sex, central corneal thickness, corneal refractive power, anterior chamber depth, lens refractive power, lens thickness, nuclear lens opacity grade, and axial length as independent variables, refractive error was

significantly associated with lower corneal refractive power ($P < 0.001$), deeper anterior chamber ($P < 0.001$), less marked nuclear lens opacity ($P < 0.001$), lower refractive lens power ($P < 0.001$), higher lens thickness ($P < 0.001$), and shorter axial length ($P < 0.001$; Table 6). The standardized correlation coefficients β were highest for the associations with shorter axial length ($\beta = -1.26$) and lower refractive lens power ($\beta = -0.95$), followed by lower corneal refractive power ($\beta = -0.76$), higher lens thickness ($\beta = 0.30$), deeper anterior chamber ($\beta = 0.28$), and less marked nuclear lens opacity ($\beta = -0.05$). In a similar manner, Pearson's correlation coefficients were highest for lens grading (Pearson's correlation coefficient, $r = -0.44$) and lens refractive power ($r = -0.43$), followed by axial length ($r = -0.37$), whereas central corneal thickness ($r = 0.09$), anterior chamber depth ($r = -0.06$) and corneal refractive power ($r = -0.05$) showed the lowest Pearson's correlation coefficients. If anterior chamber depth due to its strong relationship with axial length was not included in the multivariate analysis, similar results were obtained, with the highest standardized correlation coefficient β for axial length ($\beta = -1.09$), followed by lens refractive power ($\beta = -0.84$), corneal refractive power ($\beta = -0.66$), lens thickness ($\beta = 0.25$), and nuclear lens opacity ($\beta = -0.08$).

A stepwise multiple regression analysis of ocular refractive error as the dependent variable showed that, after adjustment for age and sex, the correlation with the ocular biometric variables increased significantly ($P < 0.001$) in each step, adding crystalline lens power ($r = 0.51$), followed by axial length ($r = 0.73$), then corneal refractive power ($r = 0.89$), and anterior chamber depth ($r = 0.92$).

When the study population was divided into subjects with a high degree of nuclear lens opacity (grade 6 or 7) and the remaining subjects with a lower grade of nuclear lens opacity, the subjects with a more marked nuclear cataract were significantly ($P < 0.001$) more myopic, a thinner lens ($P = 0.001$), and higher crystalline lens power ($P < 0.001$; Table 7). In the subgroup with a lower degree of nuclear lens opacity, the standardized correlation coefficients (β) for the associations with ocular refractive error, after adjustment for age and sex,

TABLE 3. Correlation of the Refractive Error of the Eye with Ocular Biometric Parameters in the Participants of the Central India Eye and Medical Study, Aged 50+ Years, after Adjustment for Age and Sex (Univariate Analysis)

Parameter	Crude Regression Coefficient B	95% CI for B	Standardized Correlation Coefficient β	<i>P</i>
Central corneal thickness	0.005	0.002 to 0.008	0.08	<0.001
Anterior chamber depth	-0.31	-0.59 to -0.02	-0.05	0.04
Axial length	-0.90	-1.01 to -0.78	-0.35	<0.001
Refractive lens power	-0.30	-0.33 to -0.27	-0.41	<0.001
Nuclear lens opacity	-0.97	-1.09 to -0.86	-0.42	<0.001
Corneal refractive power	-0.10	-0.16 to -0.04	-0.08	0.001
Lens thickness	0.16	0.001 to 0.33	0.04	0.048

TABLE 4. Correlation of the Amount of Nuclear Lens Opacity with Ocular Biometric Parameters Participants of the Central India Eye and Medical Study, Aged 50+ Years, after Adjustment for Age and Sex (Univariate Analysis)

Parameter	Crude Regression Coefficient B	95% CI for B	Standardized Correlation Coefficient β	P
Refractive error	-0.14	-0.16 to -0.12	-0.32	<0.001
Central corneal thickness	-0.001	-0.002 to 0.00	-0.03	0.15
Lens thickness	-0.07	-0.14 to -0.01	-0.05	0.02
Axial length	0.06	0.01 to 0.10	0.05	0.01
Crystalline lens power	0.06	0.05 to 0.07	0.19	<0.001
Corneal refractive power	0.01	-0.01 to 0.03	0.02	0.42
Anterior chamber depth	0.03	-0.08 to 0.14	0.01	0.64

were the highest for axial length ($\beta = -0.35$; $P < 0.001$), followed by lens refractive power ($r = -0.18$; $P < 0.001$), corneal refractive power ($r = -0.12$; $P = 0.01$), and anterior chamber depth ($r = -0.07$; $P < 0.001$). In the subgroup with a higher degree of nuclear lens opacity, the correlation coefficients for the associations with refractive error were the highest for lens refractive power ($\beta = -0.49$; $P < 0.001$), followed by axial length ($\beta = -0.38$; $P < 0.001$), whereas all other ocular biometric variables were not significantly associated with the refractive error of the eye (Fig. 4). In the subgroup with less marked nuclear cataract, the refractive lens power was significantly ($P < 0.001$) lower in hyperopic subjects (mean, 24.25 D; 95% CI, 24.02–24.47) and significantly ($P < 0.001$) higher in myopic subjects (25.88 D; 95% CI, 25.36–26.42) compared with emmetropic subjects (24.86 D; 95% CI, 24.69–25.04). The same held true in the marked nuclear cataract subgroup (grades 6–7) after adjustment for age and sex.

DISCUSSION

In this analysis of adults with an age of 50+ years after adjustment or age and sex, refractive error was best correlated, as assessed in standardized correlation coefficients, with crystalline lens refractive power and nuclear lens opacity grade, followed by axial length, and finally by corneal refractive power and anterior chamber depth. In multivariate analysis, the most important determinants of ocular refractive error were shorter axial length ($\beta = -1.26$), lower refractive lens power ($\beta = -0.95$), and lower corneal refractive power ($\beta = -0.76$) and, to a minor degree, higher lens thickness ($\beta = 0.30$), deeper anterior chamber ($\beta = 0.28$), and less marked nuclear lens opacity ($\beta = -0.05$). If the study population was stratified by the amount of nuclear lens opacity, in the subgroup with a higher degree of nuclear lens opacity, the refractive error of the eye after adjustment for age and sex again correlated best with refractive lens power ($\beta = -0.49$; $P < 0.001$) and axial length ($\beta = -0.38$; $P < 0.001$). In the subgroup with a lower degree of nuclear lens opacity, the correlation coefficients for the associations with refractive error were the highest for axial length ($\beta = -0.35$; $P < 0.001$),

followed by lens refractive power ($\beta = -0.18$; $P < 0.001$). Variations in refractive error in adults aged 50+ years were mostly influenced by variations in axial length and in crystalline lens refractive power, followed by variations in corneal refractive power, and, to minor degree, by variations in lens thickness and anterior chamber depth. The reasons may be potentially greater variations in crystalline lens refractive power and greater variations in axial length than variations in other ocular biometric components.

These results agree with the findings of two previous population-based studies that reported crystalline lens power calculations for adults (Iribarren G, et al. *IOVS* 2010;51:ARVO E-Abstract 1717).¹⁰ In both previous studies, negative correlations between the refractive lens power and the refractive error of the eye were found, with hyperopic eyes having lower refractive lens power than emmetropic or myopic eyes. The findings of all three studies on adults contrast with the results of studies on children whose hyperopic eyes have a higher crystalline lens power than emmetropic or myopic eyes.³

Our study confirms a previous report of a significant negative correlation between refractive lens power and both axial length and refractive error.¹⁰ It also confirms that, in eyes without significant nuclear lens opacity, hyperopic eyes have lower crystalline lens power. This apparent contradiction between the negative correlations of higher crystalline lens power with shorter axial length but with more myopic refractive error has been discussed.¹⁰ Olsen proposed to consider the combination of each of the ocular components in any given eye to understand its optics, irrespective of these paradoxical correlations.¹⁰ In fact, a negative correlation with higher lens power and shorter axial length, as shown in Figure 3, was described early in the last century, showing that eyes with longer axial lengths had lower refractive surfaces, especially in the emmetropic range.^{21–24} The development of a negative correlation between lens power and refractive error with ageing may be explained by changes in the crystalline lens, if some emmetropes are slowly driven in the hyperopic direction by a loss of refractive lens power.

Previous studies have shown that the refractive error of children and young adults is primarily influenced by variations

TABLE 5. Multivariate Analysis of the Association between Refractive Power of the Lens and Ocular Biometric Parameters in Participants of the Central India Eye and Medical Study, Aged 50+ Years

Parameter	Crude Regression Coefficient B	95% CI for B	Standardized Correlation Coefficient β	Variance Inflation Factor	P
Age	-0.01	-0.03 to 0.00	-0.03	1.44	0.054
Sex	-0.51	-0.69 to -0.32	-0.08	1.16	<0.001
Lens thickness	1.30	1.15 to 1.45	0.26	1.03	<0.001
Axial length	-2.32	-2.43 to -2.20	-0.65	1.29	<0.001
Refractive error	-0.91	-0.96 to -0.86	-0.66	1.44	<0.001
Nuclear lens opacity	0.16	0.05 to 0.28	0.05	1.65	0.007

TABLE 6. Analysis of the Association between Refractive Error of the Eye and Ocular Biometric Parameters in Participants of the Central India Eye and Medical Study, Aged 50+ Years

Parameter	Crude Regression Coefficient B	95% CI for B	Standardized Coefficient β	Variance Inflation Factor	P
Age	-0.01	-0.006, 0.001	1.46	0.19	-0.003
Sex	0.006	-0.05 to 0.06	0.001	1.21	0.84
Central corneal thickness	0.001	0.00 to 0.001	0.01	1.07	0.12
Corneal refractive power	-1.04	-1.06 to -1.02	-0.76	1.91	<0.001
Anterior chamber depth	1.83	1.74 to 1.91	0.28	1.21	<0.001
Lens refractive power	-0.69	-0.70 to -0.68	-0.95	1.69	<0.001
Lens thickness	1.12	1.08 to 1.17	0.30	1.16	<0.001
Nuclear lens opacity	-0.11	-0.15 to -0.07	-0.05	1.63	<0.007
Axial length	-3.25	-3.30 to -3.20	-1.26	2.71	<0.001

in axial length.^{21,25,26} In contrast, in this study of adults aged 50+ years, the principal determinant of refractive error was the refractive lens power, followed by axial length. Since corneal power is largely stable after the first 2 years of life^{4,5} and as axial length is generally considered to be stable after an age of 20 to 30 years,⁵ later changes in the relationship between ocular components of refraction may be predominantly due to changes in crystalline lens power. The hyperopic shifts found between ages 30 to 60 may be due to changes in the lens.⁶ Later, as nuclear opacity develops, the crystalline lens in some older individuals apparently gains power, thus increasing the prevalence of myopia in cataract subjects.

The mechanisms, by which the lens can lose or gain power in different individuals, at different ages and stages of nuclear opacity, are possibly related to its internal structure. The crystalline lens grows throughout life,¹⁻² adding new fibers under its epithelium, and as these fibers become older, they are compacted in the deeper layers of the lens. This apposition of new fibers and compaction of the older ones generates a progressive gradient of water content and of refractive index, such that the central part of the lens has less water and a greater refractive index. The power of the crystalline lens depends both on its superficial curvatures and on its internal structure, including the steepness of the gradient refractive index profile. As the lens changes its shape from adolescence to senescence, its front and back curvatures increase which would tend to result in a higher refractive power.^{12,13} Simultaneously, however, the profile of the refractive index becomes steeper with ageing as has been shown by magnetic resonance studies,²² and thus, losing the gradient, the lens loses power.²³ These two contradictory changes must balance out to produce age-related changes in lens power. The hyperopic shift in refraction seen with ageing may depend on a mismatch of these changes.⁶ The decrease in internal power caused by changes in the gradient index by compaction of the cortex was described as early as 1864 by Donders²⁴ and has even recently been postulated as a cause of presbyopia.²³

TABLE 7. Biometric Measurements in Participants of the Central India Eye and Medical Study with an Age of 50+ Years

	Nuclear Lens Opacity Grades		
	1-5	6-7	P
n	1244	641	
Spherical equivalent, D	+0.59 ± 1.47	-1.73 ± 2.52	<0.001
Corneal power, D	43.99 ± 1.63	43.97 ± 1.63	0.86
Axial length, mm	22.59 ± 0.81	22.78 ± 0.91	<0.001
Lens thickness, mm	4.03 ± 0.5	3.94 ± 0.58	0.001
Lens power, D	24.80 ± 2.53	26.77 ± 3.39	<0.001

The data are the mean ± SD and are stratified by the amount of nuclear lens opacity.

As the cataract develops, it is generally believed that the increase in the refractive index of the nucleus of the lens that is accompanied by cataract formation can lead to an increase in the internal refractive power of the lens, explaining the myopic shift seen with greater nuclear opacity. The finding in our study of a lower lens thickness in eyes with greater nuclear opacity is consistent with a greater rate of compaction and loss of water in the nucleus of cataractous lenses.^{27,28} This appears to be true even though the subjects with marked nuclear cataract were 9 years older than the subjects with a lower nuclear opacity (Table 2). The difference in age should have made their lenses thicker (and not thinner) because of the continuous formation of lens fibers, but we found the lens was 0.09 mm significantly thinner in the eyes with marked nuclear cataract. The biochemical changes leading first to presbyopia and then to cataract formation have been recently reviewed.²⁹ It is possible that these changes in cataract eyes lead to lens hardening and thinning, with loss of bound water³⁰ and an increase in refractive index that over time leads to the myopic shift observed to take place with nuclear cataract.

Potential limitations of our study should be mentioned. First, as for any population-based study, nonparticipation may be a major concern. The Central India Eye and Medical Study, however, had a reasonable response rate of 80.1%. Second, in view of the geographic and cultural diversity of India, the study population will not be representative of rural Indian populations or Indian populations in general. Since the study was focused on the associations between refractive lens power and other ocular biometric parameters and not on the prevalence of diseases, this is not a major issue. Third, the harder lenses with nuclear cataract could have had falsely low lens thickness measurements due to a potentially increased sound velocity in a harder lens. Although this possibility cannot be ruled out, a recent study had not shown an age dependency in the sound velocity in the lens.³¹

In conclusion, variations in refractive error in adults aged 50+ years were mostly influenced by variations in crystalline lens refractive power and axial length, followed by variations in corneal refractive power, and, to a minor degree, by variations in lens thickness and anterior chamber depth. Myopic subjects, in particular subjects with cataract, had a higher crystalline lens power and hyperopic subjects had a lower refractive lens power than emmetropic subjects. This finding contrasted to findings in children, who show a positive correlation between crystalline lens power and refractive error. Overall, these results suggest that changes in the crystalline lens play a major role in determining refractive error in older adults and are responsible both for hyperopic shifts during adult life and myopic shifts during the development of cataract.

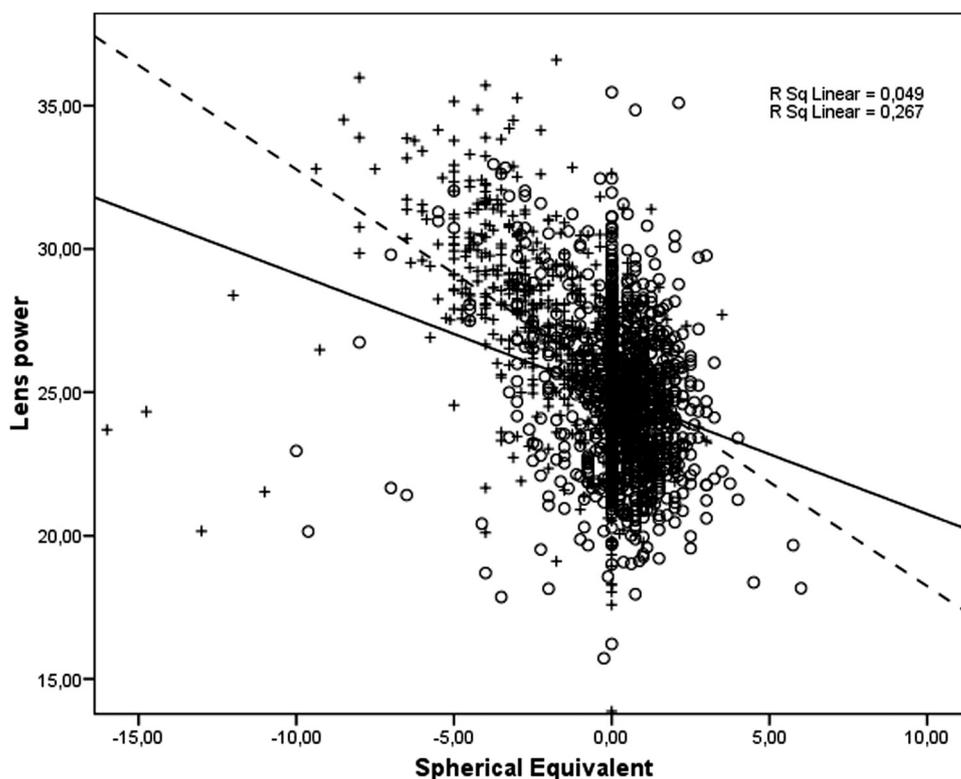


FIGURE 4. The correlation between refractive error (spherical equivalent) and the crystalline lens power in participants in the Central India Eye and Medical Study. Subjects with Marked Nuclear Cataract (grades 6 and 7, crosses and dotted regression line), had a greater negative correlation than those with less marked nuclear cataract (grades 2-5, full regression line and circles).

References

- Bron AJ, Vrensen GF, Koretz J, Maraini G, Harding JJ. The ageing lens. *Ophthalmologica*. 2000;214(1):86-104.
- Augusteyn RC. On the growth and internal structure of the human lens. *Exp Eye Res*. 2010;90(6):643-654.
- Jones LA, Mitchell GL, Mutti DO, Hayes JR, Moeschberger ML, Zadnik K. Comparison of ocular component growth curves among refractive error groups in children. *Invest Ophthalmol Vis Sci*. 2005;46(7):2317-2327.
- Sorsby A, Leary GA. A longitudinal study of refraction and its components during growth. *Spec Rep Ser Med Res Council (GB)*. 1969;309:1-41.
- Gordon RA, Donzis PB. Refractive development of the human eye. *Arch Ophthalmol*. 1985;103(6):785-789.
- Hashemi H, Iribarren R, Morgan IG, Khabazkhoob M, Mohammad K, Fotouhi A. Increased hyperopia with ageing based on cycloplegic refractions in adults: the Tehran Eye Study. *Br J Ophthalmol*. 2010;94(1):20-23.
- Sorsby A, Benjamin B, Davey JB, Sheridan M, Tanner JM. Emmetropia and its aberrations. *Spec Rep Ser Med Res Council (GB)*. 1957;293:1-69.
- Shufelt C, Fraser-Bell S, Ying-Lai M, Torres M, Varma R, Los Angeles Latino Eye Study Group. Refractive error, ocular biometry, and lens opalescence in an adult population: the Los Angeles Latino Eye Study. *Invest Ophthalmol Vis Sci*. 2005;46(12):4450-4460.
- Ip JM, Huynh SC, Kifley A, et al. Variation of the contribution from axial length and other ophthalmometric parameters to refraction by age and ethnicity. *Invest Ophthalmol Vis Sci*. 2007;48(10):4846-4853.
- Olsen T, Arnarsson A, Sasaki H, Sasaki K, Jonasson F. On the ocular refractive components: the Reykjavik Eye Study. *Acta Ophthalmol*. 2007;85(4):361-366.
- Bennett AG. A method of determining the equivalent powers of the eye and its crystalline lens without resort to phakometry. *Ophthalmic Physiol Opt*. 1988;8(1):53-59.
- Brown N. The change in lens curvature with age. *Exp Eye Res*. 1974;19(2):175-183.
- Koretz JF, Handelman GH. How the human eye focuses. *Sci Am*. 1988;259(1):92-99.
- Nangia V, Jonas JB, Sinha A, Matin A, Kulkarni M. Refractive error in central India: the Central India Eye and Medical Study. *Ophthalmology*. 2010;117(4):693-699.
- Nangia V, Jonas JB, Sinha A, Matin A, Kulkarni M, Panda-Jonas S. Ocular axial length and its associations in an adult population of Central Rural India. The Central India Eye and Medical Study. *Ophthalmology*. 2010;117(7):1360-1366.
- Age-Related Eye Disease Study Research Group. The age-related eye disease study (AREDS) system for classifying cataracts from photographs: AREDS report no. 4. *Am J Ophthalmol*. 2001;131(2):167-175.
- Fotouhi A, Morgan IG, Iribarren R, Khabazkhoob M, Hashemi H. Validity of noncycloplegic refraction in the assessment of refractive errors: the Tehran Eye Study. *Acta Ophthalmol*. 2010 Oct 26. doi:10.1111/j.1755-3768.2010.01983.x. [Epub ahead of print]
- Anderson HA, Glasser A, Stuebing KK, Manny RE. Minus lens stimulated accommodative lag as a function of age. *Optom Vis Sci*. 2009;86(6):685-694.
- Olsen T. On the calculation of power from curvature of the cornea. *Br J Ophthalmol*. 1986;70(2):152-154.
- Gullstrand, A. Appendix II: Procedure of the rays in the eye. Imagery-Laws of the first order. *Helmboltz's Handbuch der Physiologischen Optik*. Vol. 1, 3rd ed. (English translation edited by Southall JP, Optical Society of America, 1924) 1909: 350-358.
- van Alphen GW. On emmetropia and Ametropia. *Ophthalmologica*. 1961;142(suppl):1-92.
- Kasthurirangan S, Markwell EL, Atchison DA, Pope JM. In vivo study of changes in refractive index distribution in the human crystalline lens with age and accommodation. *Invest Ophthalmol Vis Sci*. 2008;49(6):2531-2540.
- Pierscionek BK. Presbyopia: effect of refractive index. *Clin Exp Optom*. 1990;73:23-30.
- Donders FC. *On the Anomalies of Accommodation and Refraction of the Eye*. London: New Sydenham Society; 1864:80-89.
- Tron EJ. The optical elements of the refractive power of the eye. In: Ridley F, Sorsby A, eds. *Modern Trends in Ophthalmology*. London: Butterworth & Co.: 1940;245-255.

26. Stenstrom S. Variations and correlations of the optical components of the eye. In: Sorsby A, ed. *Modern Trends in Ophthalmology*, Vol. 2. London: Butterworth & Co.; 1948;87-102.
27. Brown NA, Sparrow JM, Bron AJ. Central compaction in the process of lens growth as indicated by lamellar cataract. *Br J Ophthalmol*. 1988;72(7):538-544.
28. Al-Ghoul KJ, Nordgren RK, Kuszak AJ, Freel CD, Costello MJ, Kuszak JR. Structural evidence of human nuclear fiber compaction as a function of ageing and cataractogenesis. *Exp Eye Res*. 2001;72(3):199-214.
29. Truscott RJ. Presbyopia: emerging from a blur towards an understanding of the molecular basis for this most common eye condition. *Exp Eye Res*. 2009;88(2):241-247.
30. Heys KR, Friedrich MG, Truscott RJ. Free and bound water in normal and cataractous human lenses. *Invest Ophthalmol Vis Sci*. 2008;49(5):1991-1997.
31. Dubbelman M, van der Heijde GL, Weeber HA. The thickness of the aging human lens obtained from corrected Scheimpflug images. *Optom Vis Sci*. 2001;78(6):411-416.