

WORLD VIEW

Risk factors for age related cataract in a rural population of southern India: the Aravind Comprehensive Eye Study

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Aim: To determine risk factors for lens opacities and age related cataract in an older rural population of southern India.**Methods:** A cross sectional population based study of 5150 people aged 40 years and above from 50 clusters from three districts in southern India. The lens was graded and classified after dilation using LOCS III system at the slit lamp for cataract. Definite cataract was defined as nuclear opalescence ≥ 3.0 and/or cortical cataract ≥ 3.0 and/or PSC ≥ 2.0 .**Results:** Definite cataracts were found in 2449 (47.5%) of 5150 subjects and the prevalence of cataract increased with age. The age adjusted prevalence of cataract was significantly lower in males ($p = 0.0002$). Demographic risk factors—increasing age and illiteracy—were common for the three subtypes of cataract; females were more likely to have cortical cataracts and nuclear cataracts. Additionally, nuclear cataracts were associated with moderate smoking (OR: 1.28, 95% CI: 1.01 to 1.64), lean body mass indices (OR: 1.37, 95% CI: 1.17 to 1.59) and higher waist to hip ratios (OR: 0.67, 95% CI: 0.54 to 0.82); cortical cataracts with hypertension (OR: 1.39 95% CI: 1.11 to 1.72), pseudoexfoliation (OR: 1.53, 95% CI: 1.17 to 2.01), and moderate to heavy smoking; and posterior subcapsular cataracts with diabetes (OR: 1.55, 95% CI: 1.12 to 2.15), lean body mass (OR: 1.32, 95% CI: 1.11 to 1.57), and high waist to hip ratios (OR: 0.77, 95% CI: 0.62 to 0.94).**Conclusions:** Risk factors for age related cataract in this population do not appear to be different from those reported in other populations. Further studies are required to identify the reason for the high prevalence of age related cataract and to understand better the role of each risk factor for cataractogenesis in this population.

Age related cataract is the major cause of blindness in India.^{1,2} The prevalence of age related cataract and cataract surgery is higher in this rural southern Indian population than reported for most other populations studied.³ A previous study reported an earlier age of onset for age related cataract among people from the Indian subcontinent compared to other populations.⁴ Despite the public health significance of cataract in India, there are few reports on the risk factors for age related cataract from India.^{5–7} The role of environmental and personal risk factors for the development of age related cataract in this population is uncertain and may differ from that of white populations if earlier onset is indeed the case. Preventing or delaying the formation of cataract may help reduce the surgical burden on the eye care system of India. Identifying potential risk factors for age related cataract may further our understanding their role in cataractogenesis. This may help target higher risk populations for screening programmes, and develop appropriate preventive strategies. This paper reports on certain risk factors for age related cataract in a rural population aged 40 years and above in southern India.

SUBJECTS AND METHODS

The study design and methodology are described in previous publications.^{3,8} To summarise, we randomly identified 50 representative clusters from three southern districts of the state of Tamil Nadu in southern India through multistage cluster sampling. Villages of less than 350 people were excluded from the list of villages for selection since they would not produce at least 100 subjects aged 40 and older, and would not be representative of the general population of these three districts. An additional consideration was the need to conserve resources and minimise lengthy travel to

very small villages where there would be very few eligible subjects. Demographic details of eligible respondents in the selected clusters were collected by trained social workers after a door to door enumeration. All subjects aged 40 years and above were invited to the base hospital for a comprehensive ocular examination. Three levels of informed consent were used in this study, community, household, and individual. Before both screening and definitive examinations, the study was explained in detail to all potential participants and their voluntary consent was solicited. We insured that all subjects thoroughly understood the informed consent. We did not obtain thumbprints as this was problematic because many villagers could not read. All informed consent was thus verbally obtained, as a significant proportion of this population is illiterate. The study was approved, and annually re-approved, by the committee on human research at the Johns Hopkins Bloomberg School of Public Health and by the ethics review committee of the Aravind Eye and Children's hospitals. This investigation adhered to the tenets of the Declaration of Helsinki.

Trained social workers enumerated residents of households in the selected villages between 1994 and 1996.⁸ These workers were trained at Aravind Eye Hospital, Madurai, for data collection using the instruments developed for the study before the onset of the main study. Such training included collection of information from patients presenting to the hospital, staff at the hospital, and from people residing in villages near the hospital in a simulated study environment. In the field, workers collected demographic and other

Abbreviations: BMI, body mass index; LOCS, Lens Opacities Classification System; PSC, posterior subcapsular cataract; PXF, pseudoexfoliation

information on medications and personal history for subjects aged 40 years or older before any ocular examinations. All subjects aged 40 and older were transported to the Aravind Eye Hospitals in either Madurai or Tirunelveli for a comprehensive ophthalmological examination that included measurements of presenting and best corrected visual acuity, subjective retinoscopic refraction, automated full threshold visual fields for subjects with best corrected visual acuity better than 6/60 using the C-24-2 full threshold program on the Humphrey 650 visual field analyser (Dublin, CA, USA), evaluation of pupillary response, external and anterior segment examination at the slit lamp biomicroscope, measurement of intraocular pressure with a Goldmann applanation tonometer (three independent readings in each eye), and gonioscopy using a Goldmann lens. After these examinations, pupils were dilated using either 1% tropicamide and/or 10% phenylephrine unless otherwise contraindicated by gonioscopy. Subjects who had gonioscopic evidence of narrow angles and whom we felt were at risk for an attack of acute angle closure glaucoma had a laser peripheral iridectomy before dilatation of the pupils. We graded the lens at the slit lamp using the Lens Opacities Classification System (LOCS) III.⁹ The standard set of photographs were mounted next to the slit lamp for grading. We recorded the presence and degree of nuclear opalescence and colour, cortical and posterior subcapsular cataracts. We graded nuclear cataracts with reference to standard photographs on a decimal scale of 0.1–6.9 based on optical density without reference to lens colour. Cortical opacity was graded on a decimal scale of 0.1–5.9 according to the opacity that obscured the light reflex on retroillumination. Posterior subcapsular cataract (PSC) was graded according to the estimated area of posterior capsule involved. Measurements of the greatest vertical and horizontal dimensions of the PSC were made and graded on a decimal scale of 0.1–5.9. A team of ophthalmologists standardised to each other and to a gold standard examiner graded the lens. Study ophthalmologists were standardised to the lens grading on three separate occasions: once immediately before the onset of the study, and at 6 and 12 months into data collection. The ophthalmologists were standardised between themselves as well as to a senior ophthalmologist considered the gold standard. We considered a weighted kappa score of less than 0.75 as requiring re-standardisation of the ophthalmologists with respect to lens grading. For this analysis, we defined cataract as nuclear opalescence ≥ 3.0 and/or cortical cataract ≥ 3.0 and/or PSC ≥ 2.0 .

Assessment of potential risk factors

Potential risk factors assessed as part of this study included a history of smoking, diabetes, hypertension, body mass index, waist to hip ratios, and pseudoexfoliation (PXF).

We defined systemic hypertension as either a measured systolic blood pressure ≥ 160 mm Hg and/or a diastolic blood pressure ≥ 90 mm Hg or current use of systemic antihypertensive medications. We have used this definition so that we can better compare our results to those of other studies on eye diseases. We measured the blood pressure of each study participant with a mercury column sphygmomanometer (Diamond Co Industrial Electronics and Allied Products, Electronics Cooperative estate, Pune, Maharashtra, India) using a standardised technique. Subjects were rested at least 5 minutes in a seated position before measuring the blood pressure. All blood pressure measurements were made on the left arm of each study subject, using a cuff of appropriate size at the level of the heart. The radial pulse was felt and the cuff level inflated 30 mm Hg above the level at which the radial pulse disappeared and deflated slowly. The first and fifth Korotkoff sounds were recorded as systolic and diastolic

blood pressure respectively. Diabetes was defined in this study as a measured postprandial blood sugar of ≥ 180 mg/dl or current use of blood sugar lowering medications. We measured the height of subjects using a measuring tape and weight using platform scales. We used height and weight measurements of individual subjects to calculate body mass index (BMI), which was defined as weight in kilograms/height in metres squared. We classified subjects as lean if the BMI was < 20 for males and < 19 for females; as normal if the BMI was between 20–25 for males and between 19–24 for females; as overweight if the BMI was between 25–30 for males and between 24–29 for females; and obese if the BMI was > 30 for males and > 29 for females. We elicited a history of smoking; data regarding the number of cigarettes smoked per day was elicited for both current and past smokers. For this analysis, we categorised cigarette smoking as non-smokers (never smoked), mild (up to 25th percentile of person years smoked), moderate (25–75th percentile), and heavy (> 75 th percentile). We did not, however, elicit a history for passive smoking or for pipe smoking (pipe smoking is extremely rare in this population). We measured waist and hip measurements for subjects to derive the waist to hip ratios. We categorised the waist to hip ratios as normal if they were ≤ 0.8 for females and ≤ 1.0 for males.¹⁰

We diagnosed PXF by the presence of typical white deposits on the anterior lens surface and/or iris; additional sites where we found PXF included the cornea, anterior vitreous face, posterior capsule, and even intraocular lens in cataract operated eyes. Before dilatation, we looked for PXF deposits on the corneal endothelium, iris, and iris margins using a detailed high magnification slit lamp assessment. After dilation, we examined the anterior lens surface using a narrow slit lamp beam under full illumination and high magnification to scan the lens left to right focusing on detecting early signs of PXF including pregranular radial lines as well as established granular deposits. We also looked for changes in the angle using gonioscopy including increased pigmentation, PXF deposition, and PXF material within the angle.

Statistical analysis

We used Stata statistical software version 7.0 (College Station, TX, USA) for analysing data. We selected the eye with the highest cataract score for statistical analysis in people who had no previous cataract surgery. We used the phenotype of the cataract in the eye with the worst score for analysis in a person with cataract in both eyes; and in the eye with cataract for a person with cataract in one eye and no cataract in the fellow eye. We assumed the worst score for an operated eye if a person had previous cataract surgery in one eye with cataract in the fellow eye. Because we did not have access to surgical records that could give us information as to cataract phenotype at surgery, we analysed this subgroup separately with those subjects operated on for cataract in both eyes. We performed bivariate and multivariate analyses by subject to look for associations between cataract and potential risk factors using multiple logistic regression models separately for nuclear, cortical, posterior subcapsular, and mixed cataracts; all variables were included in the model as categorical variables. We used decades of years to adjust for age in our analysis. We assessed interactions between the different variables in the multiple logistic regression models and considered interactions to be significant if the *p* value was < 0.05 . Prevalence estimates, odds ratios (OR), and 95% confidence intervals (95% CI) are presented. Confidence intervals for prevalence estimates and odds ratios from the regression analyses were calculated taking into account design effects (deff) associated with cluster sampling using generalised estimation equation.

Table 1 Odds ratios (95% CI) on multivariate analysis for different cataract subtypes (nuclear, cortical, and PSC); subjects aged 40 years and older

	N = 2449 (%)	Nuclear (n = 2236)	Cortical (n = 717)	PSC (n = 1124)	Any cataract† (n = 2642)	Cataract operated (n = 482)
Age (years)						
40-49	325 (13.3)	1.00	1.00	1.00	1.00	1.00
50-59	817 (33.4)	6.90 (5.80 to 8.20)*	4.22 (3.15 to 5.66)*	4.16 (3.25 to 5.34)*	6.7 (5.7 to 8.0)*	4.00 (2.62 to 6.11)
60-69	976 (39.8)	22.22 (18.18 to 27.16)*	9.06 (6.79 to 12.09)*	11.22 (8.78 to 14.34)*	39.4 (31.1 to 49.8)*	13.38 (8.96 to 19.98)
70	331 (13.5)	18.34 (13.92 to 24.18)*	12.26 (8.72 to 17.24)*	15.14 (11.23 to 20.42)*	96.2 (59.8 to 154.5)*	25.39 (16.41 to 39.30)
Sex						
Female	1314 (53.6)	1.00	1.00	1.00	1.00	1.00
Male	1135 (46.4)	0.79 (0.65 to 0.96)*	0.76 (0.59 to 0.97)*	0.86 (0.69 to 1.07)	0.78 (0.63 to 0.97)*	1.04 (0.78 to 1.39)
No hypertension	2035 (83.1)	1.00	1.00	1.00	1.00	1.00
Hypertension	414 (16.9)	1.07 (0.88 to 1.29)	1.39 (1.11 to 1.72)*	1.20 (0.98 to 1.46)	1.00 (0.84 to 1.29)	0.97 (0.74 to 1.27)
No diabetes	2307 (94.2)	1.00	1.00	1.00	1.00	1.00
Diabetes	142 (5.8)	1.68 (1.21 to 2.34)*	1.12 (0.77 to 1.65)	1.55 (1.12 to 2.15)*	2.46 (1.70 to 3.57)*	1.60 (1.07 to 2.40)
Normal body mass index	719 (29.3)	1.00	1.00	1.00	1.00	1.00
Lean	1577 (64.4)	1.37 (1.17 to 1.59)*	1.18 (0.97 to 1.43)	1.32 (1.11 to 1.57)*	1.32 (1.12 to 1.55)*	0.87 (0.70 to 1.10)
Overweight	133 (5.4)	0.75 (0.56 to 1.01)*	1.38 (0.96 to 1.93)	1.09 (0.77 to 1.53)	0.83 (0.62 to 1.13)	1.11 (0.71 to 1.74)
Obese	20 (0.8)	0.71 (0.36 to 1.38)	0.41 (0.12 to 1.35)	1.01 (0.46 to 2.19)	0.87 (0.45 to 1.70)	1.16 (0.46 to 3.17)
No PXF	2205 (90.0)	1.00	1.00	1.00	1.00	1.00
PXF	244 (10.0)	1.26 (0.94 to 1.68)	1.53 (1.17 to 2.01)*	1.25 (0.97 to 1.61)	3.37 (2.14 to 5.62)*	2.43 (1.83 to 3.22)
Non-smoker†	1790 (73.5)	1.00	1.00	1.00	1.00	1.00
Mild smoker	120 (4.9)	1.15 (0.82 to 1.61)	0.97 (0.62 to 1.52)	0.87 (0.59 to 1.27)	1.20 (0.83 to 1.73)	1.08 (0.67 to 1.73)
Moderate	305 (12.5)	1.28 (1.01 to 1.64)*	1.36 (1.01 to 2.04)*	1.01 (0.77 to 1.32)	1.20 (1.05 to 1.57)*	0.65 (0.44 to 1.0)
Heavy	219 (9.0)	1.06 (0.81 to 1.38)	1.46 (1.05 to 2.03)*	1.00 (0.74 to 1.39)	1.1 (0.83 to 1.49)	0.74 (0.49 to 1.12)
Illiterate	1255 (51.5)	1.00	1.00	1.00	1.00	1.00
Literate	1183 (48.5)	0.50 (0.43 to 0.59)*	0.70 (0.58 to 0.85)*	0.74 (0.63 to 0.89)*	0.41 (0.36 to 0.49)*	0.70 (0.55 to 0.88)
Waist:hip ratio‡						
Normal	453 (18.6)	1.00	1.00	1.00	1.00	1.00
High	1983 (81.4)	0.67 (0.54 to 0.82)*	0.93 (0.73 to 1.18)	0.77 (0.62 to 0.94)*	0.58 (0.47 to 0.71)*	0.88 (0.65 to 1.16)

*p<0.05.

†Includes any cataract and previously cataract operated in any eye cohort.

‡Smoker categories based on quartiles of person cigarette years smoked.

§High waist to hip ratio=>0.8 for females, and >1.0 for males.

RESULTS

Definite cataract in one or both eyes was present in 2499 (47.5%) of 5150 the subjects. The age adjusted prevalence (adjusted to US population estimates for the year 2000) of definite cataract in this population was 61.9% (95% CI: 60.6 to 63.3), indicating that our population had a younger age structure than that of the United States. In those eyes with cataracts, nuclear cataract ($n = 2236$, 43.5%) was the most common type of cataract; cortical cataract was present in 717 (13.9%), posterior subcapsular cataract in 1024 (19.9%), and mixed cataracts were present in 1167 (47.7%).

The prevalence of definite age related cataracts of all types increased significantly ($p < 0.001$) with increasing age, from 15.7% among those aged 40–49 years to 79.4% among those aged ≥ 70 years. The odds ratio (95% CI) for definite cataract for age groups 50–59, 60–69, and ≥ 70 (reference category 40–49 years) were 1.3 (1.1 to 1.4), 4.3 (3.7 to 5.0), and 3.8 (3.0 to 4.8), respectively. After adjusting for age, males had lower odds (odds ratios 0.8, 95% CI: 0.7 to 0.9, $deff = 1.0$) for cataract than females. The odds ratio for cataract was significantly lower for literate subjects (OR: 0.5, 95% CI: 0.4 to 0.6, $deff = 2.5$), after adjusting for age and sex.

Cataract surgery in one or both eyes had been performed for 482 (9.4%) people including 153 people who had bilateral cataract surgery (31.7% of all subjects having had cataract surgery). The prevalence of cataract surgery in either eye increased with increasing age ($p < 0.001$).

The most common location for cortical lens opacities was the lower nasal quadrant ($n = 799$, 57.2%). Even among 235 eyes with minimal cortical changes between 0 to 1 LOCS III grade, the most common location was the lower nasal ($n = 130$, 55.3%), and lower temporal segment ($n = 95$, 40.4%).

We found hypertension (OR 1.3, 95% CI: 1.1 to 1.6, $deff = 1.4$), diabetes (OR 1.9, 95% CI: 1.4 to 2.6, $deff = 1.2$), and PXF (OR 4.6, 95% CI: 3.7 to 5.6, $deff = 0.5$) to be associated with cataract on bivariate analysis. Cataract was associated with subjects with lean body mass (OR: 1.7, 95% CI: 1.4 to 2.1, $deff = 3.1$) on bivariate analysis. We found a protective effect for cataract (OR: 0.8, 95% CI: 0.6 to 0.9, $deff = 0.8$) among those who never smoked on bivariate analysis. We found a protective effect for cataract among those with higher waist to hip ratios (OR: 0.8, 95% CI: 0.7 to 0.9, $deff = 4.1$)

There were no significant interactions between variables in the multiple logistic regression models. Multivariate analysis for nuclear cataract showed an association with increasing age, sex, illiteracy, moderate smoking, lean and overweight body mass indices, and a higher waist to hip ratio (table 1). Multivariate analysis for cortical age related cataract showed an association with increasing age, female sex, illiteracy, moderate and heavy smoking, hypertension, and PXF. Multivariate analysis for PSC showed an association with increasing age, illiteracy, diabetes, lean body mass indices, and high waist to hip ratios.

DISCUSSION

The lack of adequate epidemiological information on risk factors for age related cataract in India makes it difficult to determine if the large magnitude of cataract is essentially due to an increased predisposition to cataracts in this population, or entirely due to inadequate surgical rates. Such information is essential to develop preventive strategies even as eye care programmes in India are beginning to improve capacity in order to deal with the huge backlog without compromise on quality. Our results do not suggest the presence of environmental or personal risk factors for age related cataract peculiar to this population that have not been reported from other large population based studies.^{11–19} We also did not find any occupational link to cataract formation as over 90% of our population were primarily agricultural workers.⁸

Our study was not designed to prospectively evaluate details pertaining to nutritional intake and ultraviolet light exposure. To assess ultraviolet light exposure as a risk factor for cataract, ocular exposure measurements should be taken, and we did not have the resources to obtain such measurements in this study. We intentionally chose not to use a questionnaire as most questionnaires are not able to capture this information with accuracy primarily owing to the high potential for recall bias. Using a questionnaire in this specific illiterate and agrarian population probably would not have provided us with valid data. The alternate of measuring serum nutrient levels is also a one time measure that may not give a true picture of the nutritional status of a person over time, and may not be reflective of the possible nutritional stresses on the lens that produce cataract. We are limited by the absence of antioxidant measurements and dietary history to explore if there are differences in nutritional status that can explain the higher prevalence of age related cataract in this population.

The association of lower body mass index with increased risk for cataract has also been previously reported from India.⁴ Moderate calorie intakes has been shown to delay the formation of cataract in animal studies, the proposed biological mechanism being lower energy intake that prolongs the antioxidant or proteolytic capabilities of the lens.²⁰ BMI also affects glucose levels; higher glucose levels are associated with a higher risk for cataract.²¹ It is possible that the association of cataract with lower BMI is confounded by lower socioeconomic status, diarrhoeal diseases, or micronutrient deficiency. It is possible that the biological mechanisms that associate BMI with cataract are similar with respect to waist to hip ratios. In models where both BMI and waist to hip ratios were present, low BMI and waist to hip ratios were independently associated with increased risk of cataract, indicating that there may be several nutritional pathways to increased cataract risk.

It is not clear if the nutritional deficiency status precedes cataract formation or possibly accelerates cataract progression, or is a consequence of the reduced vision associated with cataracts that has a bearing on the earning potential of the person, and consequently food intake. It is possible that

Table 2 Population attributable risk of potentially modifiable risk factors for age related cataract in this population

Risk factor	Relative risk	Population attributable risk (%)
Hypertension	1.14	2.11
Diabetes	1.36	1.59
Smoking	1.02	0.62
Lean body mass index	1.32	15.78

there may be nutritional stresses over the life period of people in the Indian subcontinent that predisposes them to cataracts and may also possibly explain the earlier onset of cataracts in this population. The earlier and higher prevalence of cataracts among migrant Indians compared to the local population reported from United Kingdom²² suggests that factors other than the environment including nutrition or genetic factors may be involved in cataractogenesis for people from the Indian subcontinent.

Previous studies have reported lower educational levels associated with higher prevalence of age related cataract.^{4 11-13} We found similar results with illiteracy associated with age related cataract of any type. The biological association between education and cataracts is not clear. It is possible that low education is confounded by several variables including exposure to sunlight, hygiene, illnesses, and nutritional factors among others. Previous studies have reported lower surgical coverage for people with less education in this population.^{23 24}

We found moderate to heavy smoking associated with nuclear and cortical cataracts in our study. A previous clinic based case-control study from India, however, reported no association between smoking and age related cataract.²⁵ It is not clear if this difference between the two studies is related to study populations—ours was a population based sample. The difference may also be due to a possible dose-response relation relating to differences in type of cigarettes used and numbers smoked per day between urban and rural residents. We are unable to determine if this is indeed so as our study population was entirely rural in character. Previous population based studies have also reported an association between smoking and cataracts, especially nuclear cataracts.¹⁶⁻¹⁹

We explored the possibility of PXF as a risk factor for age related cataract as both PXF and cataracts are age related.²⁶ We found PXF to be significantly associated with cortical cataracts in our study population. The association between cortical cataracts and UV-B light exposure has been reported previously²⁷; however, our study was not designed to explore this possible association. We, instead, looked at the location of cortical changes as a possible indicator of an association with UV-B radiation in this population. We found cortical changes to be most commonly located in the inferior-nasal quadrant supporting a possible association with UV-B radiation. This finding concurs with previous studies in the United States and elsewhere.^{28 29} To explore this association further, we also looked at the location of minimal cortical changes (cortical changes <1.0); we found these changes to be more in the inferior nasal quadrant. We do not believe that this is because of ease of view by the examiners as all pupils were widely dilated, making it unlikely that any superior opacities would be hidden by the upper eyelid.

We found that posterior subcapsular cataracts were relatively common in this population. We do not feel that this is a result of examiner error or bias as all examiners were well versed in using the LOCS III instrument and were continuously standardised

It is possible that the higher prevalence of age related cataracts in India is entirely attributable to the low surgical coverage.^{23 30} However, the prevalence of cataract surgery among Indians aged more than 40 years is reported to range from 9.5% to 13.7% compared to 3.8% for a population in the same age group in Melbourne, Australia.³¹⁻³³ We do not think that the lower odds of having a cataract for males is the result of the higher surgical rate for males. We have previously found a comparable surgical rate for males and females in this population.³

Smoking remains a modifiable risk factor for age related cataracts in this rural southern Indian population, along with changes in lifestyle including maintaining an optimal body

mass index and waist to hip ratios that reduce the risks for diabetes and/or systemic hypertension (see table 2). Lean body mass indices were more probably associated with cataracts than obese body mass indices. It is therefore not surprising that higher waist to hip ratios are protective for cataract, although our study was not designed to determine any biological basis for this observation. Even though the regression model implies there are associations with lifestyle variables, the attributable risks are not large. The largest attributable risk was for lean body mass but since the direction of the association is unclear, these risk factors do not hold much promise for controlling the cataract problem.

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