Prevalence and risk factors of pre-senile lens opacities in the 1969-73 Vellore Birth Cohort

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Abstract

Purpose

To estimate the prevalence and determine predictors of lens opacities (LO) among South Asian Indians aged 41-44 years.

Methods

This cross sectional study included 1080 participants from the Vellore Birth Cohort, Vellore, South India. All individuals underwent anthropometric measurements, detailed ophthalmic examination including assessment of LO by LOCS III classification; and biochemical metabolic measurements. 'Any cataract' was defined as any opacity type with a score of >2 or evidence of cataract surgery in either eye. Questionnaire based assessments included information on ocular history, life-style factors, socio-economic and educational status, cooking fuel and sunlight exposure. Multivariable logistic regression analysis was used to examine the association between risk predictors and LO.

Results

The mean age (SD) of participants was 41.8 (1.0) years; 53.8% were male and 50% were rural residents. The overall prevalence of 'any cataract' was 13.8% (148/1075); 95% confidence interval (CI) (11.8,16.0); 59.1% (51.1, 67.4) had nuclear, 16.9% (11.2, 23.9) had cortical, 4.1%(1.5, 8.6) had posterior sub capsular, 18.9% (12.9, 26.2) had mixed cataracts; and 0.7% (0.02, 3.7) were pseudophakic.

Increased risk for LO was observed with a history of asthma (aOR 4.51; 2.1, 9.7), HbA1C of ≥6.5% (adjusted or aOR 2.29; 95%CI 1.4, 3.7), hypertension (aOR 1.73;1.1, 2.7) and, in a subgroup (n= 372), lower 25(OH) vitamin D levels (≤20 ng/dL)(aOR 5.56; 2.3, 13.2).

Conclusions

A higher prevalence of LO at a younger age in South Asian Indians predicts earlier onset. History of asthma, higher HbA1C, hypertension and lower 25(OH) vitamin D levels were associated with LO.

INTRODUCTION

The global increase in population and life expectancy have led to an increase in the number of people who are blind, from 36 to 43.3 million, despite a reduction in the global prevalence.(1, 2) Age related cataract (lens opacity, LO), accounts for almost 40% of all blindness and 28% of all moderate and severe visual impairment (VI), with higher and lower proportions in Asia and Africa, respectively.(2, 3) The Global Burden of Disease Study ranks cataract blindness among top the ten causes of years lived with disability from non-communicable disorders.(4, 5) Recognized risk factors for LOs include advancing age, specific ethnic groups such as South Asians(6, 7) and modifiable risk factors such as low socio-economic status, smoking, ultraviolet light exposure, obesity, asthma, hypertension and underlying metabolic disorders (diabetes).(8) In Asian Indians, the onset of LOs is earlier than in high income countries (9, 10), which may reflect earlier onset of ageing (11) and higher prevalence of metabolic risk factors.(12, 13)

LOs have a multifactorial etiology, with genetic and environmental factors interacting to increase oxidative stress in the lens. Higher levels of hydrogen peroxide, superoxide (o2-) and hydroxyl (OH) free radicals in the lens and aqueous humor are associated with LO.(14) Cells in the lens proliferate throughout life and LOs reflect a lifetime of insults, including oxidative stress.(7) However, randomized clinical trials of antioxidant vitamin supplements (i.e., A, C and E) have not shown any beneficial effects on the incidence or progression of LOs. (15) There is less evidence of whether vitamin-D deficiency/insufficiency is associated with LOs.

The purpose of this study was to estimate the prevalence of pre-senile LOs amongst adults aged 41–45 years and to examine the association between LOs and a range of socio-demographic and biomedical risk factors.

METHODS

Participants for the current study were traceable members of a subset of the Vellore Birth Cohort (VBC) in which all infants born to women in defined areas of Vellore town and three adjoining rural villages in Tamil Nadu, India, between 1969 and 1973 were included. Subsequently 10,670 singleton live births were followed up during infancy, adolescence and adulthood.(16)

Study population

This was a cross-sectional study of adults aged 39–44 years from the Phase-6 follow-up (2013-14) of VBC recruited from one urban and three rural areas nearby. The cohort is described in detail elsewhere.(17)

Study participants

One thousand and eighty of the 2218 traced cohort members were included (Fig. 1).(17) Non-participants (1,138) had either died (n = 62), were not willing to participate (n = 42), were not traced (n = 82), study area not included (n = 452) or had migrated (n = 500).

Trained health workers collected data on socio-demographic status, life-style characteristics (smoking, alcohol consumption) and daily hours of sunlight exposure in participants' homes using questionnaires. A household asset score was used as a surrogate for Socio Economic Status (SES), based on whether the household had/owned the following: electricity, fan, bicycle, radio, motorized two-wheeled vehicle, gas stove, television, cable television, electric mixer, grinder, air cooler, washing machine, car, air conditioner, computer, television antenna and telephone. A composite score was created using weights from principal component analysis (PCA)(18) and grouping the first principal component by quartiles.(19)

Educational status (using seven levels from no schooling to professional degree), was categorized "up to middle school" and "high school and above". Smoking status was defined as current smokers of cigarettes or 'beedis'. Current alcohol consumption was defined as consumption of any local or imported spirits, beer or wine. The main type of fuel used for cooking in their household was noted. Work-related activity was classified on a six-point scale ranging from 'almost entirely sedentary' to 'heavy physical work'. Additional time spent in domestic activities (e.g. sweeping, washing clothes etc.) and leisure activities (e.g. jogging, yoga) was recorded. Distances walked and cycled with and without a load were recorded, converted into approximate amount of time spent and period of time for each activity was then multiplied by metabolic constants derived from the relative energy expenditure of different activities and cumulated to arrive at a physical activity score.(20)

Ophthalmic history and examination

Participants attended a special clinic in the Department of Ophthalmology at CMC, Vellore. Ocular history was taken (night blindness, as a sign of vitamin A deficiency, previous ocular surgery or trauma, spectacle use by the participant, one or both parents or siblings, eye drop use). Distance visual acuity (VA) (uncorrected, presenting and best corrected after retinoscopy and subjective refraction), was measured using a self-illuminated logMAR visual acuity chart at 4 meters, and near vision was tested using a log MAR chart for near vision at 40 cm. Presenting VA in the better eye for distance was categorized according to World Health Organization (WHO) as 'good' (≥6/12), ' mild VI (< 6/12–6/18), 'moderate VI' (< 6/18–6/60), 'severe VI (< 6/60 to 3/60) or blind (< 3/60) after conversion to Snellen equivalents. Good near vision was defined as a corrected acuity of N8 equivalent (log MAR 1.0 M) or more in the better eye.

A comprehensive ophthalmic examination was performed by a trained ophthalmologist using a Haag Streit slit lamp which included: the intraocular pressure (IOP) measurement using Goldman Applanation tonometry; dilated fundus examination using a 90 D (Volk) lens, and grading LOs using a Lens Opacities Classification System III (LOCS) standard plate.(21) Axial length was measured using ultrasound biometry (Ocuscan, ALCON).

'Any cataract' was defined as significant LO or evidence of cataract surgery in one or both eyes. Using LOCS III classification significant LO was defined as a score of > 2 for each type of opacity i.e., for nuclear opalescence (NO), nuclear colour (NC), cortical opacity (CO) or posterior sub-capsular opacity (PSCO); NO or NC of > 2 was reported as NC. Those with more than one type were classified as 'mixed LO'. If a participant was pseudophakic/aphakic in one eye, the LOCS III grading in the other eye was used. Pseudophakia/aphakia was used if both eyes had undergone cataract surgery, or if the unoperated eye had a LO score of ≤ 2. If one eye had a condition precluding assessment of LOCS III or evidence of unilateral injury then scores from the other eye were used.

Clinical parameters and biochemical evaluation

Anthropometry included measurements of height, weight, waist circumference (WC), hip circumference (HC) and blood pressure (BP) using standard protocols. Body mass index (BMI) was calculated as the ratio of weight (kg) to height (m^2). We used WHO definitions for underweight, normal, overweight and obesity.(17) The average of three measurements was used in the analysis. Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg and diastolic blood pressure (DBP) ≥ 90 mmHg and/or being on medication for hypertension.(22) Blood samples were assayed for fasting plasma glucose by hexokinase method, lipids by colorimetry using Roche Chemistry analysers and glycosylated haemoglobin (HbA1C) by HPLC using Biorad Variant II. Diabetes was defined as HB A1C of ≥6.5%.(23) Serum 25(OH) vitamin-D levels were measured by electrochemiluminescence assay using Cobas e170 in a subset of 372 participants on whom values were available as they were taking part in another study at the same time.(24) Serum levels ≤ 20 ng/dL were categorised as deficient.(25)

Statistical analysis

Participants' characteristics are presented as means with standard deviation (SD) for normally distributed variables; median (inter-quartile range; IQR) for skewed variables, and proportions for categorical variables. Baseline characteristics are summarized using two sample t-tests and chi-square tests stratified by gender and place of residence. Risk factors for LO were chosen on the basis of clinical importance. Univariate and multivariable logistic regression analyses were used to study predictors of LO and the results are presented as odds ratios (OR) and 95% confidence intervals (CI). All variables were entered simultaneously in the multivariate model which included age, gender, education and current smoking, alcohol consumption, household possession score, hours outdoor, cooking fuel used, history of asthma, HbA1c, hypertension, body mass index, axial length and physical activity score. A subgroup analysis (n = 374) was undertaken to explore the association between serum 25(OH) vitamin D levels and LO in individuals on whom 25(OH) vitamin D was measured.(24) All statistical analyses were performed using Stata/IC version 16 (StataCorp. 2019. College Station, TX: LLC).

The study adhered to the guidelines of the Declaration of Helsinki and was approved by the ethics committees of Christian Medical College, Vellore (IRB min no.7765 dt 22 /2 /2012) and Public Health Foundation of India. All participants provided informed consent. Participants with undiagnosed diabetes or with ocular morbidity requiring treatment were referred to the respective clinics in CMC.

RESULTS

A total of 1,080 traced cohort members who agreed to participate were examined; five were excluded (two had history of bilateral injury and three had missing LOCSIII data) leaving 1075 for analysis (Figure 1).

The mean age (SD) of participants at examination was 41.8 (1.0) (range 41-44) years and 53.8% (n=578) were male (Table 1). The mean BMI (SD) was 25.4 (4.8) kg/m^2 (in the overweight range). More urban men (38.0%) were overweight than rural men; urban women had the highest proportion (70.2%). Men from rural and urban residential areas had higher educational status than women. Only men reported smoking (32.5%) and consuming alcohol (45%). Urban men and women had higher SES scores than their rural counterparts. Women had higher physical activity scores than men, and urban and rural women spent longer outside the home than their male counterparts. Most participants (80%) used liquid petroleum gas (LPG) as a cooking fuel. Approximately 3% had a history of asthma, 12.5% had an HbA1c of ≥6.5% and 21.7% had hypertension.

General ocular findings

Family history of spectacle use / holding things close to see was reported in one or both parents by 26.1%, in sibling alone in 4.5%, children alone in 2.5% and a combination of more than one first degree relative in 16.8% of participants. Reported spectacle use for near alone, distance alone and for both was 7.7%, 5.5% and 2.2% respectively. Self-reported ocular history included trauma in either eye [33, 3.1%], night blindness [6, 0.6% (mostly women)], surgery in either eye for cataract, glaucoma, or trauma [8, 0.7%] and current use of eye drops [8, 0.7%]

Among the 1065 participants with VA data, 95% had ‘good’ VA, 2% had mild VI and 3% had moderate VI; 99.7% had normal near vision with correction. The mean (SD) IOP was 13.7 (2.8) mm Hg.

Lens opacities

The overall prevalence of ‘any cataract’ was 13.8% (95% CI 11.8, 16.0) [men: 15.1% (12.2,18.2); women: 12.3% (9.5,15.5)]. Combining gender and place of residence the prevalence was as follows: rural men, 17.3% (50/289), urban women 14.2% (35/247), urban men 13.2% (38/288), and rural women 10.4% (26/250). There was no significant difference by sex (p=0.16) or place of residence (p=0.83). Nuclear cataract was the commonest type of LO (59.1%; 95% CI 51.1, 67.4) followed by cortical (16.9%; 95% CI 11.2, 23.9), posterior subcapsular (4.1%; 95% CI 1.5, 8.6) and mixed opacities 18.9% (95% CI 12.9, 26.2). Only 0.7% (95% CI 0.02, 3.7) were pseudophakic in both eyes.

In unadjusted logistic regression analysis, higher household asset scores and higher educational status were significantly associated with LO, but were not significant in the multivariable model. The following remained statistically significant in the multivariable model: higher HbA1C (OR 2.29; 95% CI 1.4, 3.7), hypertension (OR 1.73; 95% CI 1.1, 2.7) and a history of asthma (OR 4.51; 95% CI 2.1, 9.7). However, further adjustment for waist circumference (p=0.23) or waist hip ratio (p=0.04) did not show any greater effect on LO (data not shown). In the subgroup analysis of 372 individuals, LOs were significantly associated with low 25(OH) vitamin D levels (OR 5.56; 95% CI 2.3, 13.2) (p<0.001)(Table 2). The population attributable risk of LO from vitamin D deficiency was 56%. A sensitivity analysis comparing the sub-group with vitamin D data (n=372) with those without (n=703) showed no significant differences in several characteristics except education and type of LO. However, those without vitamin D levels were better educated (high school and above; 48.4% versus 48.1%, p=0.01) and had a higher prevalence of any LO (15.5% versus 10.5%, p=0.02)..

The representativeness of participants studied in 1998-2002 was compared with an earlier cohort. (20) To assess the representativeness of participants in our study from cohort members studied in 1998-2002 (n=2218), the age, gender, place of residence, educational status and SES among those examined in the current study (2013/2014) were compared with those who were not. There were no significant differences in age (p= 0.1), sex, (p=0.21) and educational status (p =0.10). There were significant differences only in place of birth (rural/urban; (p<0.001) and SES (p <0.001)(Supplemental Table 1).

DISCUSSION

Lens opacities increase over the age of 50 years and only a few studies have reported the prevalence of LO among individuals aged less than 50 years (Table 3).(26-37) Our prevalence estimate (13.8%) is comparable to the south Indian Aravind Comprehensive Eye Study (AECS), which used similar methods (age range 40–49 years, 15.7%),(36) but higher than in a Chinese study of 45-49 year olds (5.9%,95%CI 4.9-7.0).(30) The prevalence of LOs using the LOCS II grading of 2 or more in the Barbados Eye studies (age range 40-49 years) were between 3.0 and 4.7%.(26, 29, 38) Comparing prevalence estimates between studies needs caution, due to methodological differences in the definitions and classification systems used for LOs (Table 3). However, the prevalence does seem to be lower in high-income countries than in middle-income countries, which may be explained by lower exposure to modifiable risk factors, such as lifestyle factors, and better control of blood glucose amongst people with diabetes.

In our study, nuclear LOs were the commonest type (8.1%), which is similar to other Indian studies such as AECS (8.2%),(36) but higher than in the Andhra Pradesh Eye Disease Survey (APEDS)(3.5%).(39) In high-income countries cortical LO are commoner in both younger and older populations.(29) Different LO types may be associated with specific risk factors, the most commonly reported being cortical LO and high UVB exposure.(40) However, in our study the number of participants with LOs were too few for analysis by type of LO.

Men had a slightly higher prevalence of LO than women, but this was not statistically significant. This differs from other studies where women generally have a higher prevalence, particularly those done earlier.(29, 41, 42) Reasons for the gender difference are not fully understood, but may be due to a fall in oestrogen-mediated anti-ageing effects on the lens in women.(43) Less pronounced gender differences in LO in younger populations were also reported from the Swedish national cataract register.(44)

The Beaver Dam Eye Study showed a U-shaped relationship between SES and cataracts, with higher frequencies at extremes of SES,(45) reflecting different exposure to risk factors amongst those very poor and very affluent. Our study did not show any significant relationship with SES, despite a detailed SES assessment using multiple indicators such as household assets and education. This is in contrast to APEDS, where the prevalence of LOs was higher among those with a lower SES based on monthly income.(39) The different indicators used to calculate SES may explain the differences.

The absence of an association between current smoking and LO in our study is similar to other studies undertaken in East Asia,(41, 46) but differs from other studies in India(39, 42). A recent meta- analysis showed that ‘ever smokers’ had a higher risk of cataract in both cohort and case control studies.(47) Current exposure to biomass cooking fuels also did not show any significant association, which differs from other Indian studies(48) possibly because participants in our study were exposed to fewer cumulative years of biomass smoke due to the use of gas for cooking. Though there is evidence to link cigarette smoking and exposure to biomass smoke with LOs, and the reversibility of early changes if the exposure was removed, (49) as oxidative damage generated by smoke constituents is thought to be an important mediator.(50), we were unable to examine this with our data.

The increased risk of LO among individuals with asthma has been reported previously,(51, 52) which may reflect steroid use. In a large general practice study in the United Kingdom, (n=201,816; age 3-90 years), corticosteroid use was associated with increased cataract risk (relative risk 1.3) but this was not evident in those under the age of 40 years.(53) Our study lacked information on duration of steroid exposure, nevertheless our results reinforce the risk associated with history of asthma and LO.

Previous studies show variable associations between obesity and LOs.(41, 54, 55) Pooled estimates from a meta-analysis of 17 studies, including one from Asia, demonstrated a 2% increase in age-related cataracts with every 1kg/m^2 increase in BMI for PSC only, but the pooled effect showed a weak association.(56) In our study, there was no significant difference in cataract prevalence between individuals who were underweight, overweight and obese (Table 2). However, an insignificant, marginal increase was seen with higher quartiles of waist circumference and waist-hip ratio (data not shown).

Our finding that individuals with higher HbA1C are associated with greater risk of LO concurs with other studies(41, 42, 54, 57) reinforcing that hyperglycaemia is an important risk factor for LO. This is attributed to increased osmotic and oxidative stress and non-enzymatic glycation of lens proteins(58)

The high prevalence of overweight and obesity, and diabetes compared with other populous countries was also reported in the Phase 5 VBC study.(17) The prevalence of diabetes in our cohort was also higher than other NCD-RisC estimates for India, with little difference between rural and urban populations.(17) In India, the number of people with diabetes is predicted to increase to more than 130 million by 2045,(59) which is likely to further increase the burden of diabetic retinopathy and cataract. In India, the age of onset of diabetes is generally lower than in other populations, which may in part be explained by the “thin-fat” Indian phenotype.(60) India is also undergoing rapid urbanization, with easy access to unhealthy food and reduced levels of physical activity.(61) Considering the inadequate resources for diabetes care and eye care, India faces a huge public eye health problem.

A meta-analysis reported hypertension to be a risk factor for LO, particularly posterior subcapsular opacities.(16, 62) Some pathogenetic mechanisms have been postulated, the most likely being inflammatory, but findings are not consistent across studies. Our estimates (aOR 1.73, 95% CI 1.1, 2.7) are comparable to the findings of a meta-analysis of cohort studies (RR 1.08; 95% CI: 1.05–1.12) and case-control or cross-sectional studies (OR 1.28; 95% CI: 1.12–1.45).(62) Hypertension is also an important risk factor for diabetic retinopathy and could exacerbate the increase in avoidable blindness from cataract and diabetic retinopathy. (59)

Despite other studies of sunlight exposure and cataract showing a modest association, including in India, (63) sunlight exposure was not significantly associated with LO in our study. This may reflect underestimation of sunlight exposure which was questionnaire based and prone to recall bias.

In the subgroup analysis, vitamin-D deficiency gave a 5-fold higher odds of LO, which has been reported to a weaker extent in other studies,(64-67) for example in South Korean men(67) and in younger women in the USA.(66) Vitamin D deficiency is more frequent in individuals with pigmented skin, lower midday sunlight exposure and those who live at higher latitudes.(67, 68) Photoxidation of lens proteins(69) and altered calcium signaling are implicated in cataractogenesis.(70) LOs in vitamin-D deficiency may be mediated through reduced antioxidant activity,(67) and alteration in calcium homeostasis.(71) Lower levels of vitamin D have also been detected in aqueous and vitreous humor in patients with cataract than those with retinal diseases .(72) To our knowledge, this is the first study to show such a strong association between vitamin D deficiency and any cataract in young adults, and further studies are warranted.

This is the first observational study of a birth cohort, which provides insights into early ageing manifested by early onset of LOs. The relatively large sample size with rich phenotype and risk factor data adds strength to the study and allows for further follow-up studies of eye conditions. Our study may be limited by selection bias, which is inherent in longitudinal cohort studies where participants can be hard to trace. The absence of association with some of the recognized risk factors for LO, such as smoking and sunlight exposure in our cohort, suggests the need for more accurate exposure assessments, and exploration of dose responses.

Rapid socioeconomic development in India, with changing lifestyles, leading to more obesity, hypertension and diabetes, is likely to increase the burden of cataract blindness in younger adults with alarming public health implications. Modifiable risk factors need to be addressed through eye health promotion, which needs to be integrated into policies and programs for the control of NCDs.

In conclusion, the prevalence of LOs in this birth cohort was higher than in many other studies, but similar to another study in south India. Nuclear cataracts were the commonest form of cataract. A history of bronchial asthma, hypertension and hyperglycemia were significantly associated with LOs. The strong association between lower serum vitamin D levels needs further investigation in India, as it is a potentially modifiable risk factor.

Declarations

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Authorship Contribution statement:

All authors contributed to the research ; BA, CG , GVSM , NJ, PP, AB, TK, RI, LMA, AA, NT, TP, GA were involved in the design of the study; PP, BA, NM, JPC, FJ, HYC were responsible for data collection; PP, BA, PS, HYC, MG, SKV, CG were responsible for data analysis and drafted the manuscript. All authors reviewed the manuscript and the interpretations, and approved of the final version.

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Tables

Table 1: Characteristics of the study population and risk factors for lens opacities, by sex and place of residence

Variables	Male (n=578)		Female(n=497)		Male vs female	Rural vs urban
	Rural (n=289)	Urban (n=289)	Rural (n=249)	Urban (n=248)	p value	p value
Age (mean, SD) years	41.9 (0.9)	41.5 (1.0)	42.0 (0.9)	41.7 (1.0)	0.182	<0.001
Educational status (N, %)					<0.001	<0.001
Up to middle school	136 (47.1)	122 (42.2)	173 (69.5)	125 (50.4)		
High school and above	153 (52.9)	167 (57.8)	76 (30.5)	122 (49.6)		
Household asset score (SES)						
1 (lowest)	109 (37.7)	42 (14.5)	112 (45.0)	40 (16.1)		
2	72 (24.9)	65 (22.5)	51 (20.5)	47 (19.0)	0.228	<0.001
3	65 (22.5)	80 (27.7)	57 (22.9)	74 (29.8)		
4 (highest)	43 (14.9)	102 (35.3)	29 (11.7)	87 (35.1)		
Body mass index(kg/m^2) (N, %) †					<0.001	<0.001
<18.5	24 (8.3)	18 (6.3)	18 (7.2)	11 (4.4)		
18.5-24.9	155 (53.6)	124 (43.1)	104 (41.8)	63 (25.4)		
25.0-29.9	94 (32.5)	108 (37.5)	85 (34.1)	96 (38.7)		
≥30.0	16 (5.5)	38 (13.2)	42 (16.9)	78 (31.5)		
Physical activity score‡ (median, IQR)	1290 (825, 1498)	1015 (780, 1410)	1758 (1438, 2114)	1640 (1333,2042)	<0.001	0.014
Smoking status (N, %)						
Yes	70 (24.2)	117 (40.5)	0 (0.0)	0 (0.0)	<0.001	<0.001
Alcohol status (N, %)					<0.001	0.003
Yes	151 (52.3)	109 (37.7)	0 (0.0)	0 (0.0)		
Hours outside home (N, %)						
1-4 hrs	109 (37.7)	35 (12.1)	160 (64.3)	58 (23.4)		
5-9 hrs	128 (44.3)	52 (17.9)	61 (24.5)	8 (3.2)	<0.001	<0.001
10 and above	52 (18.0)	202 (70.0)	28 (11.2)	182 (73.4)		
Cooking fuel# (N, %)						
Liquefied petroleum gas	206 (71.3)	255 (88.2)	184 (73.9)	214 (86.3)		
Wood	78 (27.0)	18 (6.2)	62 (24.9)	16 (6.5)	0.826	0.826
Others (kerosene, biogas)	5 (1.7)	16 (5.6)	3 (1.2)	18 (7.3)		

Hip circumference (mean, (SD) cm†	89.2 (7.2)	92.7 (8.6)	92.7 (10.3)	99.3 (11.1)	<0.001	<0.001
Waist circumference (mean, (SD) cm†	87.8 (11.1)	92.2 (12.1)	81.7 (12.0)	87.5 (11.6)	<0.001	<0.001
Waist hip ratio†	0.98 (0.06)	0.99 (0.06)	0.88 (0.08)	0.88 (0.07)	<0.001	0.25
HbA1C (N, %)	246 (85.1)	248 (85.8)	229 (92.0)	217 (87.9)	0.028	0.446
<6.5%	43 (14.9)	41 (14.2)	20 (8.0)	30 (12.1)		
≥6.5%						
Hypertension (N, %)						
Yes	77 (26.6)	84 (29.1)	33 (13.3)	39 (15.7)	<0.001	0.328
Intraocular pressure† (mean, SD)						
Right eye	13.4 (3.0)	13.9(3.0)	13.0(2.9)	13.9(2.8)	0.346	0.0002
Left eye	13.6 (3.1)	14.2(3.0)	13.5(3.0)	14.1(2.8)	0.630	0.004
Lens opacity type (N, %)						
No opacity	239 (82.7)	252 (87.2)	224 (90.0)	213 (85.9)		
Nuclear	28 (9.7)	22 (7.6)	14 (5.6)	24 (9.7)	0.522	0.709
Cortical	11 (3.8)	6 (2.1)	5 (2.0)	3 (1.2)		
Posterior	2 (0.7)	1 (0.4)	1 (0.4)	2 (0.8)		
Mixed	9 (3.1)	8 (2.8)	5 (2.8)	6 (2.4)		
Any lens opacity (N, %)	50 (17.3)	37 (12.8)	26 (10.4)	35 (14.1)	0.187	0.732

IQR = interquartile range; † Data missing for one subject

Table 2: Univariate and multivariable analysis of risk factors for lens opacity

Risk factors	Lens opacity (LOCS III) (n=1075)		Unadjusted		Adjusted#	
	Absent (n=927) n (%)	Present (n=148) n (%)	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (mean, SD) years	41.8 (1.0)	41.8 (0.9)	1.09 (0.9,1.3)	0.36	1.10 (0.9,1.3)	0.32
Sex						
Male	491 (84.9)	87 (15.1)	1.27 (0.9, 1.8)	0.19	1.17 (0.7, 1.9)	0.54
Female	433 (87.7)	61 (12.3)	1.00		1.00	
Education (N, %)						
Up to middle school	494 (88.9)	62 (11.2)	1.00		1.00	
High school and above	433 (83.4)	86 (16.6)	1.58 (1.1, 2.2)	0.01	1.34 (0.9, 1.9)	0.16
Household asset score (SES) (N, %)						
1 (lowest)	266 (87.8)	37 (2.2)	1.00	0.02	1.00	
2	209 (88.9)	26 (11.1)	0.89 (0.5,1.5)		0.71 (0.4,1.3)	0.280
3	241 (87.3)	35 (12.7)	1.04 (0.6,1.7)		0.63 (0.4,1.2)	0.16
4 (highest)	211 (80.8)	50 (19.2)	1.70 (1.1,2.7)		1.01 (0.5,1.9)	0.98
Body mass index (kg/m^2) (N, %)†						
<18.5	63 (88.7)	8 (11.3)	0.74 (0.3,1.6)	0.67	0.94 (0.4,2.1)	0.88
18.5-24.9	381 (85.4)	65 (14.6)	1.00		1.00	
25.0-29.9	336 (87.7)	47 (12.3)	0.82 (0.5,1.2)		0.64 (0.4,0.9)	0.05
≥30.0	146 (83.9)	28 (16.1)	1.12 (0.7,1.8)		0.84 (0.5,1.4)	0.54
Physical activity score, median (IQR)	1425 (1011, 835)	1320 (910, 1746)	0.99 (0.9, 1.0)	0.098	0.99 (0.9,1.0)	0.69
Current smoking (N, %)						
No	764 (86.0)	124 (14.0)	1.00		1.00	
Yes	163 (87.2)	24 (12.8)	0.91 (0.6, 1.4)	0.68	0.75 (0.4, 1.3)	0.31
Alcohol consumption (N, %)						
No	705 (86.5)	110 (13.5)	1.00		1.00	
Yes	222 (85.4)	38 (14.6)	1.10 (0.7, 1.6)	0.650	0.91 (0.5, 1.5)	0.72

Hours outdoor (N, %)						
1-4	308 (85.1))	54 (14.9)	1.00	0.84	1.00	
5-9	225 (90.4)	24 (9.6)	0.61 (0.4, 1.0)		0.56 (0.3,0.9)	0.05
10 & above	394 (84.9)	70 (15.1)	1.01 (0.7,1.5)		0.99 (0.6,1.5)	0.95
Cooking fuel used (N, %)						
Liquefied petroleum gas	736 (85.7)	123 (14.3)	2.17 (0.7,7.1)	0.20	1.75 (0.5,6.0)	0.38
Wood	152 (87.4)	22 (12.6)	1.88 (0.5,6.6)	0.32	1.99 (0.5,7.4)	0.30
Others	39 (92.9)	3 (7.1)	1.00		1.00	
History of asthma (N, %)						
Yes	20 (60.6)	13 (39.4)	4.36 (2.1, 8.9)	<0.001	4.51 (2.1, 9.7)	<0.001
No	906 (87.0)	135 (13.0)	1.00		1.00	
HbA1c (N, %)						
<6.5%	828 (88.1)	112 (11.9)	1.00		1.00	
≥6.5%	98 (73.1)	36 (26.9)	2.72 (1.8,4.2)	<0.001	2.29 (1.4,3.7)	0.001
Hypertension (N, %)				<0.001		0.015
Yes	184 (79.0)	49 (21.0)	2.00 (1.4,2.9)		1.73 (1.1,2.7)	
No (ref)	743 (88.2)	99 (11.8)	1.00		1.00	
Axial length (mm), mean (SD)	22.9 (0.9)	23.0 (1.0)	1.16 (0.9, 1.4)	0.11	1.17 (0.9, 1.4)	0.13
Vitamin D status in subgroup (n=372)						
Vitamin D (ng/ml) (N, %)						
≤20 ng/dL	126 (81.3)	29 (18.7)	4.76 (2.2,10.1)	<0.001	5.56 (2.3,13.2)	<0.001
>20 ng/dL (ref)	207 (95.4)	10 (4.6)	1.00		1.00	

† Data missing for one participant;   p-value for trend test

#All the variables listed in the left-hand column were adjusted simultaneously in the regression model.

Table 3. Prevalence of lens opacities in other population based studies reporting a similar age group

Region	Country	Year	Age group	Sample size	Rural/urban residence	LO grading system (*)	Prevalence (%, 95% confidence interval)	Commonest type of LO
AMRO	United States of America(1)	2003	40 - 49	2363	Urban	LOCS II (2/2/2)	3(2.3 – 3.7)	CO (1.7%)
AFRO	Tanzania(2)	2001	40 - 49	1339	Rural	WHO simplified grading system	4.5(3.4 – 5.6)	CO (2.4%)
AMRO	Barbados(3)	1996	40 - 49	1333	**	LOCS II (2/2/2)	4.7	CO (3.9%)
WPRO	China(4)	2012	45 - 49	1917	Rural	LOCSIII (2/2/2)	5.9(4.9 – 7)	CO (3.5%)
SEARO	Myanmar(5)	2007	40 - 49	657	Rural	LOCS III (4/2/2)	6.1(4.3 – 7)	NO (2.4%)
WPRO	Singapore Malay (6)	2004 - 06	40 - 49	813	Urban	WISCONSIN	6.2(4.5 – 7.9)	CO (4.2%)
WPRO	Singapore Chinese(7)	1997-8	40 - 49	270	**	LOCS III (4/2/2)	7	CO (3.0%)
SEARO	Sri Lanka(8)	2006-7	40 - 49	331	Rural	LOCS III (4/2/2)	9.4(6.3 – 12.5)	***
EMRO	Pakistan(9)	2007	40 - 49	3567	Urban /Rural	Mehra Minassian	10.6 (9.6 – 11.7)	***
SEARO	India, Madurai(10)	1995-7	40 - 49	2061	Rural	LOCS III (3/3/2)	15.7(14.1 – 17.3)	NO (8.2%)
SEARO	Indonesia(11)	2003	40-49	198	Rural	LOCS III (4/4/2)	24.3 (0-100)	Mixed 16%
EURO	Italy(12)	1995	40 -49	278	Urban	LOCS II (2/2/2)	4(2.8 – 5.1)	N (1.5%)
SEARO	**India, Vellore**	**2014**	**41 - 45**	**1075**	**Rural/urban**	**LOCSIII (>2/2/2)**	**13.8(11.8 – 16.0)**	**N (8.2%)**

Region: AFRO: Africa; AMRO: Americas, EMRO: Eastern Mediterranean, EURO: Europe; SEARO: South East Asia; WPRO Western Pacific

*Grading system cutoffs for nuclear /cortical / posterior sub capsular cataracts; **Not mentioned; *** Not available for this specific age group

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Figures

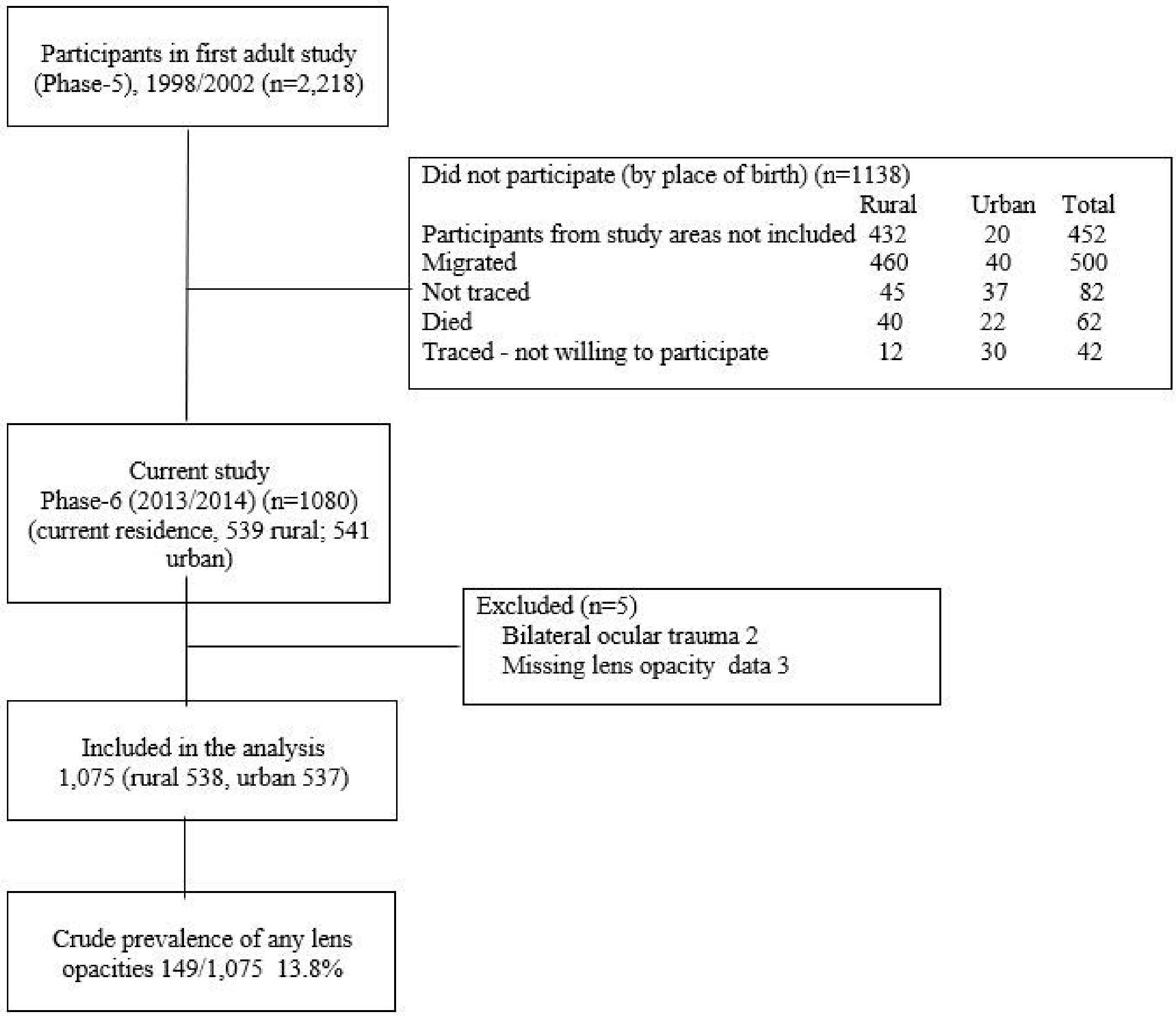

Figure 1

Flow of the study

Supplementary Files

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