



Risk Factors Associated with Cataracts in Middle-Aged People, an Incidence-Based Case-Control Study in Shiraz, Iran

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Abstract

Background: Cataracts is the most common cause of blindness worldwide. Factors that influence the development of cataracts in middle-aged people have not been thoroughly investigated.

Objectives: The purpose of this study was to explore risk factors associated with cataracts among middle-aged patients attended an outpatient clinic in Shiraz, Iran.

Methods: This was a case-control study of patients aged 40 to 59 years who were attended Motahari outpatient clinic from February to June 2017. The case subjects were 140 patients who were found to have incident cataracts and controls were 140 age- and sex-matched healthy patients with a normal eye examination. Data were collected by an interviewer-administered questionnaire, an ophthalmologic examination, and the measurement of HbA1c levels. Univariate and conditional logistic regression analyses were used to identify factors that independently predicted the risk of middle-aged cataracts.

Results: Our findings showed that a middle-aged cataracts was associated with myopia (odds ratio [OR] = 2.66, P = 0.001), a history of cataracts before age 60 years in patient's first degree relatives (OR = 2.12, P = 0.009), a low educational level (OR = 1.89, P = 0.020), and overweight or obesity (OR = 1.80, P = 0.039). Prediabetes and diabetes status were not independently associated with the outcome of interest in this age group.

Conclusions: A hereditary predisposition may play a primary role in the development of cataracts in middle-aged people. Myopia and cataracts may share a genetic predisposition in this age group. Further genetic studies are recommended to elucidate the possible role of specific genes in the development of middle-aged cataracts.

Keywords: Risk Factors, Cataracts, Middle-Aged

1. Background

Cataracts is the leading cause of blindness and is responsible for loss of sight in more than 20 million people worldwide (1, 2). Global population growth and increased human longevity have resulted in a rise in the burden of age-related cataracts, and cataracts surgery is one of the most common surgical procedures performed in the world (3, 4).

Cataracts is an important public health issue for which few modifiable risk factors have been identified and currently, the only effective treatment is surgical removal of the lens. Epidemiologic studies have investigated potential risk factors for cataracts. The most important risk factor is age and it seems that age-related cataracts is an inevitable outcome of aging (5-7). Also, there is evidence from several epidemiologic and population-based studies that both cataracts prevalence and the rate of cataracts ex-

traction is higher in females than in males (8-10). Other suggested risk factors include excessive exposure to the sun, smoking, diabetes mellitus, myopia, obesity, and steroid use (11-19).

Most previous studies have focused on risk factors for cataracts among elderly people. The best of our knowledge, no study has investigated risk factors of cataracts among Iranian middle-aged people. There are two published studies from Iran; one has specifically investigated Iranian patients with diabetes (20) and another study has focused on dietary factors in hospitalized patients with cataracts (21).

The questions which motivated this research were "why do some people develop age-related cataracts in an earlier age than others and which genetic or environmental factors may play a prominent role in the development of middle-aged cataracts?"

2. Objectives

The aim of the present study was to address factors associated with incident cataracts among middle-aged patients in an outpatient clinic in Shiraz, Iran.

3. Methods

This was a group-matched case-control study, which was carried out in Shiraz, Iran. We recruited the patients aged 40 to 59 years who attended Motahari outpatient clinic from February to June 2017. Eligible patients were considered those who had an incident diagnosis of cataracts. Eligible controls consisted of age- and sex-matched healthy patients with a normal eye examination (except for possible refractive errors) who came to Motahari clinic meanwhile the patients were enrolling. People with significant underlying ocular or systemic diseases and those with a history of eye trauma were excluded from the study.

Since we could not find a similar study in middle-aged people, we used a small group of our participants to estimate the final sample size. The sample size was calculated with the following values: alpha = 0.05, a power of 80%, standard deviation = 0.5, and the effect size = 0.2. It was estimated at 140 patients per group. The cases and controls were group-matched in terms of age and sex. Four age groups were considered, including: 40 - 44, 45 - 49, 50 - 54, and 55 - 59 years of age. According to age groups and sex of the patients, similar proportions of healthy subjects were enrolled as the control group.

The patients' characteristics included age and sex, educational level, urban/rural residence, self-reported exposure to ambient natural, and artificial radiation sources, such as self-reported mean time of sun exposure (the estimated daily time outdoors between 9:00 A.M. and 5:00 P.M.), mean time of computer use, and mean duration of smartphone use during a typical day, sunglass use, refractive myopia, overweight and obesity, tobacco smoking, diabetes mellitus, the use of certain medications, including corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), calcium channel blockers and statins, and a familial history of cataracts before the age of 60 in first degree relatives. Myopia was defined as spherical equivalent refraction equal to or more than -0.5 diopter in one or both eyes or a history of correction of myopia by surgery. Diabetic patients were defined as those who were receiving antidiabetic medications or those with HbA1c \geq 6.5. Prediabetics were those with HbA1c between 5.7 to 6.4. HbA1c levels were measured as an average estimate of plasma glucose over the preceding three months to detect patients with undiagnosed pre-diabetes or diabetes mellitus (22). A current tobacco smoker was defined as a subject who had

smoked during the past 30 days. An ex-smoker was defined as one who used to smoke tobacco, but had not smoked during the past 30 days. Never smoker was defined as one who has never smoked tobacco. Educational attainment was divided into three categories: illiterate or a primary school degree, a high school degree, and an academic degree. Medication use was defined as a history of regular use of systemic corticosteroids, NSAIDs, calcium channel blockers or statins for more than three months.

Patients' weight and height were measured and body mass index (BMI) were calculated. Overweight was defined as a BMI of 25 to 29.9 kg per square meter and obesity was defined as a BMI \geq 30 kg per square meter (23). Then the patients were examined by an ophthalmologist to diagnose refractive errors, confirm the presence or absence of cataracts, and determine the type of cataracts. Blood samples were drawn and HbA1c levels were measured.

Data were collected by an interviewer-administered data collection form by a trained interviewer. The collected data were analyzed by SPSS software, version 19 (IBM, United States). Comparisons between the patients and control subjects were made using independent *t*-test for continuous variables and by chi-square test for categorical variables. Relationships between cataracts and potential risk factors were estimated by calculating odds ratios (ORs) and the associated 95% confidence interval (CI). Stepwise backward-selection logistic regression analysis was performed to identify factors that independently predict the risk of cataracts among study participants. The significance level was considered $<$ 0.05 for all statistical analyses. This project received ethical approval from the Research Ethical Committee of Shiraz University of Medical Sciences (code: IR.SUMS.MED.REC.1394.s89).

4. Results

The cases and controls were 280 people aged 40 to 59 years residing in Shiraz who were attended Motahari clinic from February to June 2017. The mean age \pm standard deviation (SD) of the participants was 51.4 ± 5.8 . More than half (62.1%) of the participants were female, 70.3% were overweight or obese, 23.2% had a high school degree or higher and 8.2% were currently or ex-smokers. None of the study participants stated a history of ocular trauma.

Age and sex distribution of the cases and control subjects are shown in Table 1.

In both case and control groups, 41.4% of the participants were in the 55 - 59 years age group, 16.4% were in the 50 - 54 years age group, 29.3% were in the 45 - 49 years age group, and 12.9% were in the 40 - 44 years age group. The proportion of female to male subjects were equal (a ratio of 1:1) between the case and control groups (Table 1).

Table 1. Age and Sex Distribution of Study Participants^a

Case and Control Groups	Age Groups				Total
	40 - 44	45 - 49	50 - 54	55 - 59	
Female	12 (66.7)	28 (68.3)	16 (69.6)	34 (58.6)	90 (64.3)
Male	6 (33.3)	13 (31.7)	7 (30.4)	24 (41.4)	50 (35.7)
Total	18 (12.9)	41 (29.3)	23 (16.4)	58 (41.4)	140 (100)

^aValues are expressed as No. (%).

Univariate analysis of the variables of interest is shown in [Table 2](#). The mean age \pm SD of the cases was 51.55 ± 5.88 and the controls was 51.22 ± 5.77 ($P = 0.638$). The cases were more likely to have a low educational attainment (84.3%) than controls (69.3%) ($P = 0.010$). About one-third of the cases and one-fourth of the controls were rural resident ($P = 0.085$). About 75% of the cases and 65% of the controls were overweight or obese ($P = 0.058$).

The controls were more likely to wear sunglasses (16.4%) than cases (9.3%) ($P = 0.050$). There was no significant difference in mean time of sun exposure (from 9:00 A.M. until 5:00 P.M.) ($P = 0.461$), computer use ($P = 0.162$) and smartphone use ($P = 0.235$) in a typical day between the cases and controls. There was a significant association between a family history of cataracts before the age of 60 in first degree relatives of the study participants ($P = 0.037$). Diabetes ($P = 0.578$) and pre-diabetes ($P = 0.324$) were not associated with increased risk of cataracts in this age group. There was no significant association between long-term use of medications (including corticosteroids, NSAIDs, Ca-channel blockers, statins), and the development of cataracts in the population of the study ($P > 0.2$).

Among cases, the most common types of cataracts were posterior sub-capsular (44.3%), nuclear (33.6%) and cortical (22.1%), respectively. The results of backward stepwise regression analysis are shown in [Table 2](#). After adjusting for covariables, incident cataracts was significantly associated with myopia (AOR = 2.66, 95% C.I.: 1.53 - 4.63, $P = 0.001$), a history of cataracts before the age of 60 among patient's first degree relatives (AOR=2.12, 95% CI:1.28 - 3.32, $P = 0.009$), low educational levels (AOR=1.89, 95% CI: 1.18 - 3.15, $P = 0.020$), and overweight or obesity (AOR = 1.80, 95%CI: 1.03 - 3.17, $P = 0.039$).

5. Discussion

Our findings showed that low educational attainment was independently associated with middle-aged cataracts; a variable that has been consistently suggested as a risk factor for age-related cataracts. Although there is not still enough scientific explanation for this association, the dif-

ference between educational levels can be related to differences in lifestyle and environmental exposures (10, 12).

It has been reported that the prevalence of age-related cataracts is higher in rural populations and it has been linked to a higher average age, higher exposure to the sun, and lower educational levels of rural people (10, 24). In the present study, cases had more commonly a rural residence compared to control subjects, but we did not find a statistically significant association between rural/urban residence and development of cataracts in our population of the study. Similarly, a large population-based study in China did not find any significant difference in terms of cataracts prevalence between rural and urban residents (25). It seems that rural and urban people have become progressively more similar in matter of their lifestyles and environmental exposures. Also, more powerful factors may influence the development of cataracts in middle-aged people.

Many studies have suggested an association between obesity and cataracts, especially of posterior sub-capsular type (26, 27); however, evidence supporting this association has been controversial (28, 29). Similarly, our study showed that there was a significant association between increased body mass index and incident cataracts among middle-aged patients. Although the mechanism is not clear, this association is of high importance because overweight and obesity can be modified through lifestyle and nutritional measures.

Also, several studies have suggested an association between diabetes mellitus and age-related cataracts (16, 30-32). Our findings showed no significant association between diabetes and middle-aged cataracts. This may be due to relatively small sample size in the present study. However, there is some concern regarding a higher rate of ophthalmologic referral for the annual eye examination of diabetic patients that increase the chance of detection of cataracts in patients with diabetes (12).

A history of intense sun exposure, particularly in people over 40 years of age may induce cataracts formation and wearing sunglasses can greatly reduce this risk (33). We did not find a statistically significant association between estimated daily outdoor sun exposure and the risk

of cataracts. Also, there was no significant association between wearing sunglasses and cataracts development in the population of the study. Similarly, a case-control study in a Mediterranean population found no association between years of outdoor sunlight exposure and the risk of cataracts (34). Excessive sunlight exposure has been consistently associated with an increased risk of cortical cataracts, but it does not seem to significantly contribute to the development of nuclear or posterior subcapsular cataracts (35), the most common types among our population of the study.

Myopia is a known risk factor for the development of age-related cataracts (36). The associations of myopia with nuclear and posterior subcapsular cataracts have been confirmed in several studies (37). In a large prospective study, both low and high myopia were significantly associated with a higher incidence of posterior subcapsular cataracts (38). Our findings showed that there is a significant association between myopia and the development of cataracts among middle-aged patients.

Furthermore, we found that cataracts was independently associated with a history of cataracts before the age of 60 years in first degree relatives of the study participants. Our findings are consistent with epidemiological studies demonstrating more prevalent occurrence of age-related cataracts in close relatives of cataracts patients than in the general population, and genetic studies have shown the effect of specific genes in the development of cataractsous lenses (39, 40). Most genetic studies of cataracts have investigated congenital cataracts. At least one-third of congenital cataracts are hereditary. Few studies investigated genetic associations of cataracts formation in middle-aged people. The first human mutations associated with age-related cortical cataracts were identified in EPH2A, a gene encoding a transmembrane tyrosine kinase (41, 42).

One study has reported that patients with middle-aged cataracts have a higher than expected mortality rate compared with the general population, and this was explained as a consequence of a hereditary premature aging in these patients (43).

According to our findings, we suggest that genetic factors may play a more prominent role than environmental factors in the development of cataracts among middle-aged patients.

There are some potential limitations to our study. Although Motahari clinic is the largest public outpatient clinic of Shiraz, patients might have come from some limited areas of the city and this may restrict the generalizability of the results. The validity of self-reported data cannot be established and collected information is subject to bias, which is the inherence of retrospective design.

5.1. Conclusions

A hereditary predisposition may play a primary role in the development of cataracts in middle-aged people. Myopia and cataracts may share a genetic predisposition in this age group. Further genetic studies are recommended to elucidate the possible role of specific genes in the development of middle-aged cataracts.

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Footnotes

Authors' Contribution: Shahram Bamdad and Ramin Shiraly authors have contributed to designing, conducting, and preparation of the manuscript.

Conflict of Interests: The authors declare no conflict of interest.

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Table 2. Association of Incident Cataracts with Different Variables in a Group-Matched Case-Control Study in Shiraz, Iran

Variables	Case Patients (N = 140)	Control Patients (N = 140)	Unadjusted OR (95% CI)	P Value	Adjusted OR (95% CI)	P Value
Demographics						
Gender			1.0	-	-	-
Female	90 (64.3)	90 (64.3)	1.0 (0.61 - 1.63)	> 0.99	-	
Male	50 (35.7)	50 (23.7)				
Age, y, mean \pm SD	51.55 \pm 5.88	51.22 \pm 5.80		0.638		
Educational level						
An academic degree	10 (7.1)	17 (12.1)	1.0		1.0	
A high school degree	12 (8.6)	26 (18.6)	2.06 (0.90 - 4.72)	0.085	1.36 (1.10 - 3.03)	0.026
Illiterate or primary school	118 (84.3)	97 (69.3)	2.63 (1.26 - 5.49)	0.010	1.89 (1.18 - 3.15)	0.020
Residence						
Urban	93 (66.4)	107 (76.4)	1.0		1.0	
Rural	47 (33.6)	33 (23.6)	1.63 (0.97 - 2.76)	0.085	1.22 (0.68 - 2.18)	0.520
Overweight/obese^a						
No	35 (25.2)	48 (34.5)	1.0		1.0	
Yes	105 (74.8)	92 (65.5)	1.56 (0.93 - 2.63)	0.058	1.80 (1.03 - 3.17)	0.039
Smoking status^b						
Never smoker	127 (90.7)	130 (92.9)	1.0		1.0	
Current or ex-smoker	13 (9.3)	10 (7.1)	0.75 (0.31 - 1.77)	0.664	1.15 (0.44 - 3.05)	0.774
Radiation Exposure						
Sun exposure, hours per day	3.01 \pm 1.77	2.86 \pm 1.61	0.94 (0.82 - 1.09)	0.459	1.04 (0.88 - 1.23)	0.580
Computer use						
No	130 (92.9)	122 (87.1)	1.0		1.0	
Yes	10 (7.1)	18 (12.9)	0.52 (0.23 - 1.17)	0.162	1.20 (0.44 - 3.26)	0.709
Smartphone use, min/d	34.62 \pm 27.16	38.57 \pm 28.31	1.00 (0.99 - 1.01)	0.240	1.00 (0.99 - 1.01)	> 0.99
Sunglasses use						
Yes	13 (9.3)	23 (16.4)	1.0		1.0	
No	127 (90.7)	117 (83.6)	1.92 (0.93 - 3.96)	0.050	0.7 (0.31 - 1.55)	0.382
Diabetes status						
Normal	115 (82.1)	117 (83.6)	1.0		1.0	
Pre-diabetic	10 (7.1)	13 (9.3)	0.79 (0.30 - 2.08)	0.324	0.78 (0.31 - 1.97)	0.612
Diabetic	15 (10.8)	10 (7.1)	1.06 (0.48 - 2.36)	0.578	1.32 (0.53 - 3.33)	0.544
Ocular Factors						
Myopia						
No	82 (58.6)	109 (77.9)	1.0		1.0	
Yes	58 (41.4)	31 (22.1)	2.48 (1.47 - 4.19)	< 0.001	2.66 (1.53 - 4.63)	0.001
Family history of cataracts^c						
No	58 (41.4)	73 (52.1)	1.0		1.0	

Yes	82 (58.6)	67 (47.9)	1.54 (0.96 - 2.47)	0.037	2.12 (1.28 - 3.32)	0.009
Drug History						
NSAID use						
Yes	17 (12.1)	24 (17.1)	1.0		1.0	
No	123 (87.9)	116 (82.9)	0.66 (0.34 - 1.30)	0.310	0.64 (0.31 - 1.30)	0.216
Corticosteroids^d						
No	138 (98.6)	136 (97.1)	1.0		1.0	
Yes	2 (1.4)	4 (2.9)	2.02 (0.36 - 11.26)	0.684	0.51 (0.86 - 3.30)	0.460
Statins						
No	115 (82.1)	113 (80.7)	1.0		1.0	
Yes	25 (17.9)	27 (19.3)	1.09 (0.60 - 2.00)	0.878	0.87 (0.42 - 1.78)	0.705
Calcium channel blockers						
No	115 (82.1)	113 (80.7)	1.0		1.0	
Yes	27 (19.3)	26 (18.6)	0.95 (0.52 - 1.73)	> 0.99	1.05 (0.48 - 2.27)	>0.99

Abbreviation: NSAID, nonsteroidal anti-inflammatory drugs.

^aBody mass index is the weight in kilograms divided by the square of the height in meters.

^bA currently tobacco smoker is a subject who has smoked during the past 30 days. An ex-smoker is one who used to smoke but has not smoked during the past 30 days. Never smoker is a one who has never smoked tobacco.

^cHistory of cataracts before the age of 60 in first degree relatives.

^dFisher exact test was used.