Original Article

Risk Factors for Age-Related Macular Degeneration in Elderly Chinese Population in Shenyang of China*

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Abstract

Objective The paper aims to evaluate the risk factors for age-related macular degeneration (AMD) in elderly Chinese population in Shenyang, a northeast city of China.

Methods A case-control study was conducted to investigate the risk factors for the prevalence of AMD. Ninety three AMD patients diagnosed by a complete ophthalmic examination were recruited as cases from the outpatient departments of two eye hospitals in Shenyang, while 108 normal subjects of similar age and sex were recruited as controls. A questionnaire was administered among both cases and controls.

Results AMD patients aged 60 years and older accounted for 75.3%. There were significantly higher educational levels, shorter smoking history, less sunlight exposure and cataract, and higher proportion of antioxidants intake in controls than in AMD patients. The frequency of intake of fruits, legumes, fish and shrimps was significantly higher in controls than in AMD patients. In a binary logistic regression analysis, smoking and cataract were the risk factors for AMD (OR: 4.44, 95% CI: 2.27-8.69; OR: 4.47, 95% CI: 2.26-8.85 respectively). The high educational background was a protective factor for AMD (OR: 0.761, 95% CI: 0.51-0.98).

Conclusion A low educational background, smoking and cataract are associated with a higher prevalence of AMD.

Key words: Lifestyle; Dietary habit; Age-related macular degeneration; Chinese people

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INTRODUCTION

Age-related macular degeneration (AMD), the leading cause of blindness in elderly populations is becoming increasingly prevalent. The pathogenesis of AMD is likely a result of combined influences of genetic and environmental risk factors[1]. To date, the exact mechanism of macular degeneration has remained delusive. As there are currently no effective treatment strategies for most patients with AMD, attention has focused on efforts to prevent or stop the progression of AMD through optimization of modifiable risk factors such as diet and nutritional status[2-3]. Accumulating evidence implicates that oxidative stress from reactive oxygen species is one of the key factors in the pathogenesis of AMD[4].

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Therefore, a number of studies have evaluated the potential benefits of antioxidant supplementation in delaying the development and progression of AMD[5-6].

To date, smoking is the only proven modifiable risk factor for AMD[1]. Other factors include family history, body mass index, atherosclerosis, dietary habit such as higher intake of fat and lower intake of antioxidants[1,3]. The rapid industrialization of China has increased the average daily calories and fat intake in the past two decades[7]. Dietary fat and glycemic index have been reported recently to be associated with late AMD[8-9]. Epidemiological studies indicate that genetic and environmental factors that affect the prevalence of AMD may differ in different geographic regions and vary with different ethnicities[10-11]. To our knowledge, the risk factors associated with prevalence of Chinese patients with AMD, especially in lifestyle and dietary habit, have not been reported until now; and therefore, the aim of this survey was to study the factors associated with AMD, and to compare the result with findings obtained in a control group with similar age and sex, in order to identify risk factors for AMD.

MATERIALS AND METHODS

Participants

Ninety three patients with 57 dry and 36 wet AMD, aged from 45 to 80 years, were recruited between January of 2007 and January of 2008 from the outpatient department of Shenyang AIER Eye Hospital and Heshi Eye Hospital. AMD was diagnosed according to a complete ophthalmological examination including a detailed fundus examination and a fluorescent angiography and classified as the subtypes of dry and wet AMD[12]. One hundred and eight subjects with no eye disease that could cause significant or permanent loss of visual acuity were randomly selected from the same area after matching for gender and age with the cases, and served as controls. All subjects gave their written informed consent to the study which was approved by the Ethics Committee of the Faculty.

Data Collection

A detailed questionnaire was designed according to the references[1,13]. The first part of the questionnaire included demographic details, such as age, gender, weight and height. The second part consisted of questions about the associated factors of AMD, such as family history, educational level, smoking history, diseases such as cataract, diabetes mellitus and hypertension, protection in sunlight, intake of antioxidants and dietary habit.

To investigate the dietary habit, we administered a food frequency questionnaire. The food list contained items rich in micronutrients, including vegetables, fruits, poultry and meat, eggs, fish and shrimps, milk and milk products, legumes, animal liver and tea. For the convenience of computation, the frequency of food intake was converted into times per day or week (times/day or times/week) according to the Chinese Food Guideline[14]. The contents of the questionnaire are shown in the Supplementary Table.

Statistical Analysis

Statistical Package for Social Sciences (SPSS, Chicago, IL, USA) version 11.5 was used for the data analysis. Counting data were analyzed by Pearson chi-squared test, and measurement data were examined by using one-way ANOVA when assumptions of normality and homogeneity of variances were met. Risk factors were analyzed by a binary logistic regression analysis. Probabilities of 0.05 were considered to be statistically significant.

RESULTS

There was no statistically significant difference in age and sex distribution, or in body mass index between AMD patients and controls (P>0.05). The baseline characteristics of cases and controls are shown in Table 1.

Table 1. Baseline Characteristics of Cases *(n*=93) and Controls (*n*=108)

Variable		Cases	Contriols	*P* value
Gender distribution	Male	39 (41.9)	40 (37.0)	0.563
	Female	54 (58.1)	68 (63.0)	
Age(year)	45-59	23 (24.7)	35(32.4)	
	60-69	37 (39.8)	40 (37.0)	0.475
	70-80	33 (35.5)	33 (30.6)	
Body mass index		23.6±3.2	24.0±2.6	0.316

Note. Date are shown as the mean±SD or number (percentages).

There was a higher educational level attained, higher proportion of protection in sunlight and intake of antioxidants, and lower proportion of cataract and smoking in controls than in AMD patients (P<0.05). There was no significant difference

in family history, physical exercise, diabetes mellitus or hypertension between AMD patients and controls (P>0.05). The risk factors associated with AMD are shown in Table 2.

Table 2. Risk Factors Associated with AMD (n)

Variables	Evaluation	Cases	Controls	*P* value
Family history	Yes	5	4	0.568
	No	88	104	
Completed Highest educational level attained	primary education	25	10	0.001
	secondary education	37	35	
	pre-university education	18	35	
	university degree	13	28	
Physical exercise	Yes	62	69	0.680
	No	31	39	
Smoking status	Never	49	85	0.000
	Former	18	12	
	Current	26	11	
Cataract	Yes	41	26	0.003
	No	52	82	
Diabetes mellitus	Yes	18	23	0.733
	No	75	85	
Hypertension	Yes	21	27	0.688
	No	72	81	
Protection in Sunlight	Yes	22	47	0.003
	No	71	61	
Intake of antioxidants	Yes	44	67	0.036
	No	49	41	

Table 3 shows the frequency of intake of food rich in micronutrients in the past one year among AMD patients and controls. As shown in the table, the frequency of daily intake of fruits and legumes was significantly higher in controls than in AMD patients (P=0.007 and P=0.016 respectively). There was also a significantly higher frequency of weekly intake of fish and shrimps in controls (63.9%) than in AMD patients (45.2%) (P=0.008). But there was no significant difference in intake of vegetables, poultry and meat, eggs, milk and milk products, animal liver and tea between AMD patients and controls (P>0.05).

The above risk factors, which had statistically significant difference in cases and controls, were analyzed further by a binary logistic regression. The results showed that educational levels were negatively associated with AMD (OR: 0.76, 95% CI: 0.51-0.98) while smoking and cataract were positively associated with AMD (OR :4.44, 95% CI: 2.27-8.69; OR: 4.47, 95% CI: 2.26-8.895 respectively). The odd ratios (OR) and confidence intervals (CI) for risk factors associated with AMD are shown in Table 4.

Table 3. Frequency of Food Intake in the Past One Year in Cases and Controls (n, %)

		Cases (n=93)	Controls (n=108)	*P* Value
Vegetables	⩾1 times/day	87 (93.5)	93 (86.1)	0.107
	< 1 times/day	6 (6.5)	15 (13.9)	
Fruits	⩾1 times/day	57 (61.3)	85 (78.7)	0.007
	< 1 times/day	36 (38.7)	23 (21.3)	
Poultry and Meat	⩾1 times/day	33 (35.5)	47 (43.5)	0.246
	< 1 times/day	60 (64.5)	61 (56.5)	
Eggs	⩾1 times/day	37 (39.8)	38 (35.2)	0.501
	< 1 times/day	56 (60.2)	70 (64.8)	
Legumes	⩾1 times/day	23 (24.7)	44 (40.7)	0.016
	< 1 times/day	70 (75.3)	64 (59.3)	
Milk and milk product	⩾1 times/day	33 (35.5)	51 (47.2)	0.092
	< 1 times/day	60 (64.5)	57 (52.8)	
Fish and shrimp	⩾1 times/day	42 (45.2)	69 (63.9)	0.008
	< 1 times/day	51 (54.8)	39 (36.1)	
Animal liver	⩾1 times/day	7 (7.5)	9 (8.3)	0.833
	< 1 times/day	86 (92.5)	99 (92.7)	
Tea	⩾1 times/day	25 (26.9)	25 (23.1)	0.542
	< 1 times/day	68 (73.1)	83 (76.9)	

Table 4. Odd Ratios (OR) and Confidence Intervals (CI) for Risk Factors Associated with AMD by a Binary Logistic Regression Analysis

Variables	Variables	*P* Value	95% C.I
Educational levels	0.76	0.040	0.51-0.98
Smoking	4.44	0.000	2.27-8.69
Cataract	4.47	0.000	2.26-8.85

DISCUSSION

AMD accounts for the majority of irreversible severe vision loss in the elderly population[1]. The progressive loss of vision that occurs in AMD cases is a result of injury to the macular photoreceptors, retinal pigment epithelial, Bruch's membrane and the choroid[15]. This is a heterogeneous disease typically categorized as either "dry" or "wet" AMD. Dry AMD is associated with early-stage disease and subretinal deposits known as drusen that may cause little or no loss of vision. However, dry AMD may also lead to regional atrophy of the photoreceptors in the macula (called GA), with significant vision loss. Wet or neovascular AMD is a late-stage disease and always associated with substantial loss of central vision due to macular edema and scarring. The events that precipitate macular injury are not known. Several clear risk factors for the dry and wet AMD have been established, including advanced age, heredity, and smoking history, and other factors

associated with AMD are being studied now[1]. In our study, dry and wet AMD were included in one case group, and their lifestyle and dietary habit were investigated.

In the present study, AMD patients aged 60 years and older were 75.3%, while the patients of the age group of 40 to 59 years accounted for 24.7%, which indicated that the prevalence of AMD rose with age. Our findings are similar to the age profile of age-related maculopathy in the Beijing eye study[16]. There was no significant difference in family history of AMD between cases and controls, and the reason may be related to the lower awareness of AMD among the elderly Chinese population in the past and at the present.

Smoking including former and current smokers was significantly higher in cases than in controls (P=0.000) in our study. Smoking is the most important and generally acknowledged modifiable risk factor for AMD[1-2]. So people should be advised not to smoke or give up smoking because of the significant known adverse effects of smoking on health[17].

There was also significant difference in the rate of educational levels attained and cataract between the controls and the cases (Table 2). There were some inconsistent results on the relationship between educational levels and the risk of AMD[18-19]. A person, who has attained high education in this country, usually lives a better life due to better economic conditions, and may pay close attention to her or his health. Cataract and AMD are the two leading causes of visual impairment in the elderly. Today, cataract surgery is the most commonly performed surgical procedure in ophthalmology, generally resulting in good visual acuity. Studies have shown controversial results regarding the association between cataract surgery and the risk of AMD[20-21]. In the present study, we only investigated the history of cataract, excluding surgical procedure in ophthalmology between cases and controls, and the cataract was significantly associated with the risk of AMD (OR: 4.47, 95% CI: 2.26-8.85).

There was a significant difference in sunlight exposure and antioxidants supplement such as vitamin C or vitamin E or zinc between cases and controls. The findings were consistent with previous reports[22-23]. The retina is vulnerable to the damaging effects of light. Although it is not possible to establish causality between sunlight exposure and supplement with antioxidants and AMD by a case-control study, our results suggest that people should use ocular protection in sunlight and follow dietary recommendations for the key antioxidant nutrients.

The potential influence of diet on the development and progression of AMD has aroused increasing interest. The majority of the literature on diet and nutritional supplementation in AMD published in the past two years has focused on the efficacy of ω-3 fatty acids, lutein, zeaxanthin, vitamin B12 and folic acid, and the constituents of AREDS formulation[3,6]. There has not been a study on the dietary habit in Chinese AMD patients until now. In the present study, there was a significantly higher frequency of intake of fruits, legumes, fish and shrimps in controls than in cases. Fruits are rich in dietary fiber and antioxidants such as vitamin C and carotene, and good for preventing chronic diseases associated with age[24]. Legumes are excellent sources of protein, essential micronutrients and fiber, and substituting foods with legumes that are high in saturated fats or refined carbohydrates is likely to lower the risk to cardiovascular diseases and type 2 diabetes mellitus[25]. Fish and shrimps were rich in micronutrients, especially long-chain omega-3 polyunsaturated fatty acids, which is necessary for maintaining retina functions. A higher intake of omega-3 polyunsaturated fatty acids was associated with decreased risk of wet AMD[26].

A recent study showed that different kinds of meat may differently affect AMD risks. For example, a higher red meat intake was positively associated with early AMD and conversely, consumption of chicken > or =3.5 times/week versus <1.5 times/week was inversely associated with late AMD[27]. In our study, the frequency of intake of poultry and meat >or=1 time/ day was not significantly different between the cases and the controls, because the specific kind of meat or the amount was not recorded, which deserves a further study. Animal foods such as meat and eggs are rich in high quality of protein, iron and other nutrients, and intake of an appropriate amount of meat and eggs in the elderly population can improve nutritional status and increase immunity. In the present study, the frequency of daily intake of poultry such as meat and eggs was relatively lower in either cases or controls.

Milk intake was inversely associated with early AMD[28]. There was no significant difference in intake of milk and milk products, and animal liver between cases and controls in the present study. In fact, milk and animal liver are important for the elderly to maintain bone and vision health due to their being rich in calcium and vitamin A and D, which are often deficiency in Chinese diet[7]. Almost 50%-60% of the

elderly population in China do not have a daily intake of milk and milk products, and about 90% of them take animal liver less than one time a week. Our findings suggest that it is necessary to direct diet of the elderly population according to the suggestions of the Nutrition Society in China.

Although there was no significant difference in intake of tea between cases and controls, catechins in green tea might play a potential role in prevention and treatment of age-related eye diseases, like cataracts, glaucoma and macular degeneration[29]. Our study showed that tea intake was lower in the elderly Chinese population.

The factors, which have statistically significant difference between the cases and the controls, were analyzed further by binary logistic regression. The results showed that educational levels were negatively associated with AMD, and smoking and cataract were positively associated with AMD.

Despite the relatively small amount of samples in our study, our results showed that educational levels, smoking and cataract were associated with AMD. High education levels attained served as a protective factor for AMD. Smoking and cataract were risk factors for AMD.

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Supplementary Table. The Study Items in the Questionnaire

1. Aging, Gender.

2. Body Mass Index based on self-reported height and weight.

3. Educational level:

    a. Completed primary education

    b. Completed secondary education

    c. Completed pre-university education

    d. Completed university degree.

4. Physical exercise: more than 3 times/week, and 30minutes/per times for six month.

5. Smoking status: Smoker: one cigarette smoked per day for six month

    a. Never

    b. Former

    c. Current smoker.

6. Self-reported history of diseases: cataract, diabetes mellitus, hypertension.

7. Protection in sunlight: wear of spectacles, sunglasses or hats.

8. Intake of antioxidants: More than 3 months for supplyment with vitamin C or E or zinc.

9. The participants were asked about frequency of food intake. For easy to compute, the frequncy of food intake was converted into times day or week (times/day or times/week) according to Chinese Food Guideline. The food items inquired about were the following:

    a. Vegetables

    b. Fruits

    c. Fish or shrimp

    d. Poultry and meat

    e. Animal liver

    f. Eggs

    g. Legumes

    h. Milk and milk products

    i. Tea