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Prevalence and associated risk factors of age-related macular degeneration in aged 50 years and older population in Shunqing district, Nanchong

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南充市顺庆区中老年年龄相关性黄斑变性患病率及相关因素分析

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摘要

目的:了解南充市顺庆区50岁及以上人群年龄相关性黄斑变性(AMD)患病率并探讨影响AMD的相关因素。

方法:以人群为基础的流行病学调查。2013-05/10,采用分层整群随机抽样方法,抽取四川省南充市顺庆区50岁及以上人群共2242人。调查内容包括一般信息登记,体格检查,实验室检查,眼科检查。AMD的诊断标准采用AMD国际临床分级系统。采用SPSS 13.0统计学软件对结果进行分析。

结果:本研究调查实际有2097人接受全程检查,受检率为93.53%。检出AMD患者207例(283眼),总患病率为9.87%,标准化后AMD的患病率为9.73%。早期和晚期AMD患病率分别为9.25%和0.62%,其中渗出性AMD患病率为0.14%。50~59、60~69、70~79及≥80岁组的AMD患病率分别为6.38%、9.27%、14.69%、17.39%。AMD导致双侧盲及低视力患病率分别为0.48%和1.45%。晚期AMD患眼视力明显低于早期AMD患眼视力。与AMD相关的影响因素有8个,年龄、收缩压、吸烟、阳光暴露、糖尿病史、白内障手术、血清总胆固醇是AMD发生的危险因素,受教育程度是保护因素。

结论:南充市顺庆区50岁及以上人群AMD患病率为9.87%,AMD患病率随着年龄的增加呈明显增长的趋势;晚期AMD严重影响视力;AMD致病危险因素包括年龄、收缩压、吸烟、阳光暴露、糖尿病史、白内障手术、血清总胆固醇,保护因素为受教育程度。

关键词:年龄相关性黄斑变性;患病率;危险因素;流行病学

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Abstract

• AIM: To describe the prevalence of age-related macular degeneration (AMD) in aged 50 years and older population in Shunqing District of Nanchong and to investigate the associated risk factors of AMD.

• METHODS: Population-based cross-sectional of epidemiological investigation. Persons aged 50 years and older, recruited between May to October 2013, from Shunqing District of Nanchong, Sichuan province, China. Totally 2242 eligible residents who aged 50 years and older were selected using a stratified, clustered, and random sampling technique. All participants underwent a standardized interview concerning general data, physical examinations, laboratory examinations, and comprehensive eye examinations. The diagnostic criteria was followed the international clinical classification systems. The survey data were analyzed by statistical software SPSS 13.0.

• RESULTS: Totally 2242 participates, whole examination were finished for 2097 persons, with the examination rate of 93.53%. There were 207 patients (283 eyes) were diagnosed as AMD, with the total prevalence rates of 9.87% and the standardized prevalence rates of 9.73%. Early and late AMD prevalence rates were 9.25% and 0.62%, respectively, among participants, in which the prevalence of exudative AMD were 0.14%. The prevalences of AMD in the age groups of 50-59, 60-69, 70-79 and no less than 80 years were 6.38%, 9.27%, 14.69% and 17.39%, respectively. The visual acuity of late AMD was significantly worse than early AMD. The prevalence of bilateral blindness and low vision were 0.48% and 1.45% of the AMD patients. There were eight factors associated with AMD: age, systolic blood pressure, smoking, sun exposure, history of diabetes, cataract surgery and serum total cholesterol were the risk factors of AMD, while the level of education was a protective factor.

• CONCLUSION: The prevalence of AMD in Shunqing District of Nanchong was 9.87%. With the age increasing,

the prevalence rate of AMD was significantly increased. The late AMD affected vision seriously. The risk factors of AMD included age, systolic blood pressure, smoking, sun exposure, history of diabetes, cataract surgery and serum total cholesterol, and the protective factor was the level of education.

• KEYWORDS: age-related macular degeneration; prevalence; risk factors; epidemiology
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INTRODUCTION

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness among elderly residing over the age of 50 years in Western countries[1]. China is the most populous developing country in the world. With the aging of population, the prevalence of AMD in China is also increasing[2]. It is reported that there are more than 40 million AMD patients in China[3]. Population-based epidemiological studies of AMD appear in Asia for just over a decade[4-5]. That's because researchers in the past have argued that Asians have a lower prevalence of AMD than Caucasians[6]. A recent Meta-analysis shows that the prevalence of AMD in Asians at a specific age is similar to that of Westerners[7]. Some risk factors such as age, smoking have been confirmed to be related to AMD, and different researchers have great controversy over other risk factors of AMD[8-10].

At present, AMD has become one of the common blinding diseases in people aged 50 years and above in China, which seriously affects the quality of life of middle-aged and elderly patients. There is little data on the epidemiology of AMD in southwest China. Therefore, understanding the prevalence and related factors of AMD is of great significance in preventing the development of AMD.

SUBJECTS AND METHODS

The object of the study is the residents aged 50 years and above in Shunqing district, Nanchong city, Sichuan province.

Exclusion Criteria Floating population, non-permanent resident population includes perennial migrant workers and long-term migrant residents.

Written informed consent was obtained from all participants after study researchers verbally explained the purpose and procedures of the study to them. The present study was conducted in accordance with the Declaration of Helsinki, and it was approved by the Ethics committee of Affiliated Hospital of North Sichuan Medical College.

This study used AMD's incidence rate of 4.9% in our survey in the last 50y[2], The formula of sample size is calculated by simple random cluster sampling: $n = Z^2 p(1-p)/B^2$, $p = 0.049$, $B = 0.049 \times 0.25 = 0.01225$ (The prevalence error was 25%), Z=1.96 (95% confidence), Get $n=1193$, Set the sampling effect coefficient of this study to be 1.50, with a 90% test rate, the required sample size is 1988.

Adopt stratified random cluster sampling method. According to household registration data, there are 2242 permanent residents aged 50 years and above.

The survey included general demographic information registration, questionnaire, eye exams and laboratory tests. General demographic information includes name, gender, ethnicity, date of birth, address, contact information, marital status, occupation, degree of culture. The education level is divided into primary school, junior high school, high school and undergraduate. Physical examination includes height, weight, and blood pressure measurements. The questionnaire included smoking, drinking, reading time, exposure to sunlight, past medical history, and the history of eye diseases. Use the ETDRS visual chart to check vision and record the best corrective vision. A fundus photograph was taken using the KOWA nonmyd WX non-mydriatic fundus camera. The diagnostic criteria were recorded by the international AMD clinical grading system[11-12] (Table 1 and Figure 1).

Laboratory tests include fasting blood glucose, blood lipids (triglycerides, total cholesterol, low-density lipoprotein, high-density lipoprotein).

Quality Control Strict quality control measures were also applied. Before formal investigations, inspectors are trained. Randomly selected 50 people to do pre-test, consistent analysis of the diagnosis results of different inspection personnel (kappa = 0.89), the results are better consistent. All fundus photographs were divided by two physicians with associate professor or above.

Statistical Analysis SPSS13.0 statistical software was used to analyze the results. Use c^2-test for single factor analysis. Then perform multivariate unconditional logistic regression analysis on variables with statistical significance in single factor analysis. Risk factors were evaluated by calculating the ratio (odd radios, OR) and 95% confidence interval (CI). Statistical significance was set at $P<0.05$.

RESULTS

In our survey, 2242 respondents were sampled and 2097 people were actually examined with a rate of 93.53%. And 748 males (35.67%) and 1349 females (64.33%) were examined. The average age of the subjects was 63.27±9.36y. Of the total of 4194 eyes of 2097 subjects, 39 eyes could not view the fundus because of huge pterygium, severe turbidity of refractive media, pupillary membrane closure and atrophy of the eyeball.

Prevalence of Age-related Macular Degeneration The survey results showed that 207 patients (283 eyes) with AMD were detected. There were 76 cases with binocular disease and 131 cases with monocular disease. The total prevalence rate was 9.87%. Based on data from the 2010 national census population aged 50 and above for age and sex standardization, the prevalence of AMD was 9.73%. In 194 patients (268

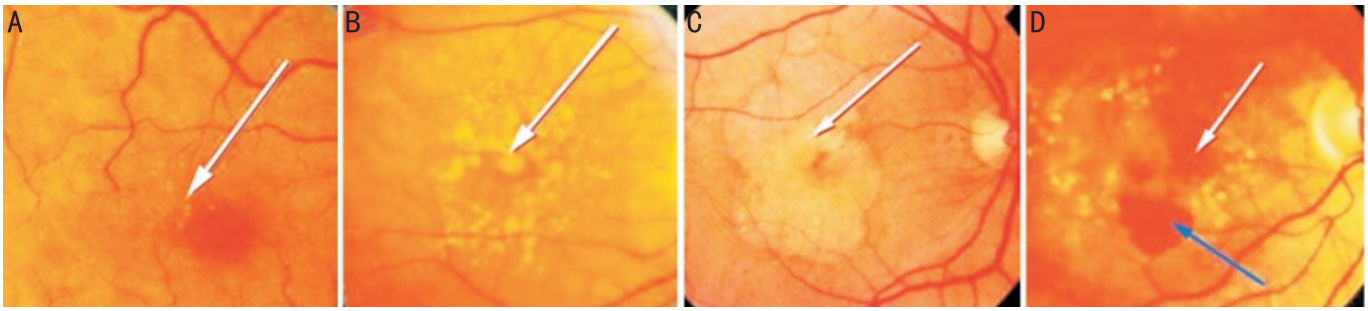

Figure 1 Classification of age-related macular degeneration (AMD) Column A shows medium-size drusen (arrows) in early AMD, and Column B shows a large druse (arrows) in intermediate AMD. In Column C, a photograph of the fundus shows geographic atrophy (white arrow). In Column D, the photograph of the fundus with neovascular age-related macular degeneration shows subretinal hemorrhage (blue arrow) and choroidal neovascularization (white arrow).

Table 1 The clinical age-related maculopathy staging system

Grade of maculopathy	Clinical features
1	No drusen or 10 small drusen without pigment abnormalities
2	Approximately 10 small drusen or 15 intermediate drusen, or pigment abnormalities associated with ARM
	2a: Drusen
	2b: RPE changes (hyperpigmentation and hypopigmentation)
	2c: Both drusen and RPE changes
3	Approximately 15 intermediate drusen or any large drusen
	3a: No drusenoid RPED
	3b: Drusenoid RPED
4	Geographic atrophy with involvement of the macular center, or noncentral geographic atrophy at least 350 μm in size
5	Exudative AMD, including nondrusenoid pigment epithelial detachments, serous or hemorrhagic retinal detachments, CNVM with subretinal or sub-RPE hemorrhages or fibrosis, or scars consistent with treatment of AMD
	5a: Serous RPED, without CNVM
	5b: CNVM or disciform scar

AMD: Age-related macular degeneration; ARM: Age-related maculopathy; CNVM: Choroidal neovascular membrane; RPE: Retinal pigment epithelium; RPED: Retinal pigment epithelial detachment. Small, drusen<63 μm in diameter located within 2 disc diameters (DDs) of the center of the macula; intermediate, drusen≥63μm but<125 μm, located within 2 DDs of the center of the macula; large, drusen≥125 μm in diameter located within 2 DDs of the center of the macula; drusenoid RPED, confluent soft drusen≥500 μm in size.

eyes) with early AMD, the prevalence was 9.25%; In 13 patients (15 eyes) with late AMD, the prevalence was 0.62%. Among them, 3 cases (3 eyes) were exudative AMD, and the prevalence rate was 0.14%. The prevalence rate of AMD was 6.38%, 9.27%, 14.69% and 17.39%, respectively, in the 50-59 group, 60-69 group, 70-79 year old group and 80-year-old group. The prevalence of AMD in different genders and ages is shown in Table 2.

Associated Risk Factors of Age - related Macular Degeneration Read the relevant literature and determine the specific research factors based on the actual situation of the survey: age, gender, education level, body mass index, systolic blood pressure, diastolic blood pressure, history of smoking and drinking, reading time, exposure to sunlight, history of diabetes and hypertension, cataract surgery, fasting blood glucose, blood lipids (including total cholesterol, triglyceride, high - density lipoprotein, low - density lipoprotein). The univariate analysis was performed for each study index of 207 patients (283 eyes) with AMD (Table 3). Multivariate logistic regression analysis was performed on the univariate analysis with statistically significant factors (gender, age, education level, systolic blood pressure, smoking, sun exposure, diabetes history, cataract surgery and serum total cholesterol). The results showed that age, systolic blood pressure, smoking, sun exposure, history of diabetes, cataract surgery, serum total cholesterol were risk factors for AMD, and education was a protective factor (Table 3).

DISCUSSION

In recent years, China's economy has developed rapidly. With the accelerating process of urbanization and the aging of the population, the prevalence of AMD has gradually increased. The prevalence of AMD epidemiological study was 3.1% - 15.5%[2,13]. The prevalence of early and late AMD reported abroad is 3.5% - 13.2% and 0.3% - 1.9%, respectively[14]. The differences between regional studies may be related to the age structure, economic conditions, geographical environment, living environment, and differences in the diagnostic and grading standards of AMD.

Table 2 Prevalence of age-related macular degeneration in different ages and genders

Age group (y)	All study subjects	Early AMD *n*(%)	Late AMD		
			GA *n* (%)	Exudative AMD *n* (%)	Any late AMD *n* (%)
Male					
50-59	162	13 (8.02)	1 (0.62)	1 (0.62)	2 (1.23)
60-69	338	33 (9.76)	0 (0)	1 (0.30)	1 (0.30)
70-79	200	29 (14.50)	2 (1.00)	1 (0.50)	3 (1.50)
≥80	48	8 (16.67)	2 (4.17)	0 (0)	2 (4.17)
Total	748	83 (11.10)	5 (0.67)	3 (0.40)	8 (1.07)
P		0.018[a]	0.029[a]	0.712	0.132
Female					
50-59	528	28 (5.30)	1 (0.19)	0 (0)	1 (0.19)
60-69	514	42 (8.17)	2 (0.39)	1 (0.19)	3 (0.58)
70-79	263	35 (13.31)	1 (0.38)	0 (0)	1 (0.38)
≥80	44	6 (13.64)	0 (0)	0 (0)	0 (0)
Total	1349	111(8.23)	4 (0.30)	1 (0.07)	5 (0.37)
P		<0.001[b]	0.753	0.857	0.725
Total					
50-59	690	41 (5.94)	2 (0.29)	1 (0.14)	3 (0.43)
60-69	852	75 (8.80)	2 (0.23)	2 (0.23)	4(0.47)
70-79	463	64 (13.82)	3 (0.65)	1 (0.22)	4(0.86)
≥80	92	14 (15.22)	2 (2.17)	0 (0)	2(2.17)
Total	2097	194 (9.25)	9 (0.43)	4 (0.19)	13(0.62)
P		<0.001[b]	0.042[a]	0.962	0.085

GA: Geographic atroph. c^2-trend test for age groups. [a]$P<0.05$, [b]$P<0.01$.

Table 3 Risk factors for AMD using univariate analysis

Characteristics	*n*(%)	AMD, *n* (%)	χ^2	*P*
Gender				
M	748 (35.67)	91 (12.17)	6.881	0.009[b]
F	1349 (64.33)	116 (8.60)		
Age (y)				
50-59	690 (32.9)	44 (6.38)	27.73	<0.001[b]
60-69	852 (40.63)	79 (9.27)		
70-79	463 (22.08)	68 (14.69)		
≥80	92 (4.39)	16 (17.39)		
Education level				
Primary school	1035 (49.35)	144 (13.91)	37.734	<0.001[b]
Junior high school	829 (39.53)	51 (6.15)		
High school	215 (10.25)	11 (5.12)		
Undergraduate	18 (0.86)	1 (5.56)		
BMI (kg/m^2)				
Normal (<25)	1592 (75.92)	168 (10.55)	3.491	0.175
Overweight (25-29.9)	475 (22.65)	37 (7.79)		
Obesity(≥30)	30 (1.43)	2 (6.67)		
Systolic pressure (mmHg)				
<120	1686 (80.40)	154 (9.13)	6.391	0.041[a]
120-139	172 (8.20)	19 (11.05)		
≥140	239 (11.40)	34 (14.23)		
Diastolic pressure (mmHg)				
<80	1879 (89.60)	188 (10.01)	0.381	0.826
80-89	205 (9.78)	18 (8.78)		
≥90	13 (0.62)	1 (7.69)		

Continued Table 3 Risk factors for AMD using univariate analysis

Characteristics	n(%)	AMD, n (%)	χ^2	P
Smoking				
Nonsmoker	1459 (69.58)	123 (8.43)	20.501	<0.001[b]
Former smoker	112 (5.34)	6 (5.36)		
Current smoker	526 (25.56)	78 (14.83)		
Drinking				
Never	1607 (76.63)	166 (10.33)	4.461	0.107
Former drinking	54 (2.58)	8 (14.81)		
Current drinking	436 (20.79)	33 (7.57)		
Reading time				
≤1h/d	1557 (74.25)	159 (10.21)	1.271	0.530
1-2h/d	504 (24.03)	46 (9.13)		
≥2h/d	36 (1.72)	2 (5.56)		
Sun exposure				
<2h/d	503 (23.99)	33 (6.56)	8.351	0.015[a]
2-5h/d	378 (18.03)	39 (10.32)		
≥5h/d	1216 (57.99)	135 (11.10)		
Diabetes				
No	1751 (83.50)	164 (9.37)	9.724	0.008[b]
≤10y	330 (15.74)	38 (11.52)		
>10y	16 (0.76)	5 (31.25)		
Hypertension				
No	1645 (78.45)	158 (9.60)	5.811	0.055
≤10y	366 (17.45)	34 (9.29)		
>10y	86 (4.10)	15 (17.44)		
Cataract surgery				
No	4146 (98.86)	275 (6.63)	7.592	0.006[b]
Yes	48 (1.14)	8 (16.67)		
Fasting blood glucose				
Normal	2003 (95.52)	197 (9.84)	3.258	0.196
Critical value	43 (2.05)	2 (4.65)		
Excessive	51 (2.43)	8 (15.69)		
Total cholesterol				
Normal	1981 (94.47)	189 (9.54)	4.400	0.036[a]
Abnormal	116 (5.53)	18 (15.52)		
Triglyceride				
Normal	1866 (88.98)	188 (10.08)	0.791	0.374
Abnormal	231 (11.02)	19 (8.23)		
High-density lipoprotein				
Normal	2075 (98.95)	206 (9.93)	0.233	0.629
Abnormal	22 (1.05)	1 (4.55)		
Low-density lipoprotein				
Normal	2015 (96.09)	202 (10.02)	1.366	0.243
Abnormal	82 (3.91)	5 (6.10)		

[a]P<0.05; [b]P<0.01.

Age is the strongest predictor of AMD, and the occurrence of AMD shows a clear upward trend with age[7,15]. Prevalence of AMD among people over 40 years of age in South Korea found that the risk of AMD increased by 8% for every one year increase in age[14]. Early and late AMD is found in 31.0% and 28.4% of individuals older than 90 years[16]. Although infrequent in people younger than 50 years, the risk of acquiring AMD increases more than twofold in patients older than 70 years compared to patients between 50 and 59 years of age[17]. The results of this study are consistent with previous studies. The prevalence of AMD in the age groups of 50-59, 60-69, 70-79 and older than 80 years were 6.38%, 9.27%, 14.69% and 17.39%, respectively. Although age is an uncontrollable risk factor, early detection and intervention can delay the progression of AMD.

At present, most studies have shown that the incidence of

Table 4 Risk factors for AMD using multivariate logistic regression analysis

Risk factors	*OR*	95% *CI*	*P*
Age (y)			
50-59	1	1	
60-69	1.510	1.034-2.211	<0.001[b]
70-79	2.633	1.802-3.854	<0.001[b]
≥80	3.197	1.882-5.834	<0.001[b]
Education level			
Primary school	1	1	
Junior high school	0.417	0.301-0.577	<0.001[b]
High school	0.344	0.187-0.635	<0.001[b]
Undergraduate	0.373	0.059-2.552	<0.001[b]
Systolic pressure (mmHg)			
<120	1	1	
120-139	1.106	0.674-1.996	0.292
≥140	1.556	1.087-1.974	0.015[a]
Smoking			
Nonsmoker	1	1	
Former smoker	0.635	0.365-1.348	0.232
Current smoker	1.981	1.469-2.650	<0.001[b]
Sun exposure			
<2h/d	1	1	
2-5h/d	1.638	1.012-2.561	0.041[a]
≥5h/d	1.749	1.195-2.583	0.004[b]
Diabetes			
No	1	1	
≤10y	1.228	0.878-1.851	0.216
>10y	3.499	1.915-11.410	0.004[b]
Cataract surgery			
Yes *vs* No	2.901	1.312-6.094	0.008[b]
Total cholesterol			
Abnormal *vs* Normal	1.514	0.911-2.828	0.045[a]

CI: Confidence interval. [a]$P<0.05$; [b]$P<0.01$.

AMD is low in people with high education degree[18]. Our study shows that education level is a protective factor for AMD. This finding is supported by other studies[19-20]. In particular, the Los Angeles Latino Eye Study pointed out that early AMD was significantly associated with less than 12y of education[20]. In general, people with higher educational level have less exposure to sunlight, less smoking, and stronger eye health care, which may be the reason for their protective factors.

Epidemiological studies have been controversial about the impact of blood pressure on AMD. Some scholars believe that high blood pressure is a high risk factor for AMD[21-22], but others believe that there is no correlation between blood pressure and AMD[23-24]. Cheung *et al*[25] considered hypertension to be significantly associated with early AMD. Erke *et al*[26] found that systolic blood pressure is associated with late AMD, Hogg *et al*[27] reached the same conclusion through case-control study. However, the Blue Mountain Eye Research Center evaluated the relationship between cardiovascular risk factors and AMD and found that neither systolic nor diastolic blood pressure was associated with AMD[28]. Our investigation shows that the history of hypertension has no correlation with AMD, but the systolic pressure is a risk factor for AMD. The result may be due to the control of hypertension in the primary hospital. Most hypertensive patients control their blood pressure within a normal range. But there are still a few patients who may not pay attention, and newly found hypertension patients, whose systolic blood pressure may be higher than normal. As to whether blood pressure is associated with AMD, long-term follow-up can be adequately assessed, and randomized controlled trials can be further studied to confirm the correlation.

A large number of epidemiological data have shown that smoking is a strong and stable risk factor for AMD[14,17,29]. Long-term smoking can increase the risk of 2-4 times[30-31]. Japanese scholars reported that the prevalence of AMD in men is higher than that in women due to the high prevalence of smoking among men[32]. Our survey shows that the current smoking population is 1.981 times more likely to have AMD than never smoking before (95% *CI* 1.469-2.650). Smoking leads to AMD through direct oxidative damage to the retina, depleting serum anti-oxidants, activating the immune system and causing hardening of the retinal arteries. In addition, smoking can induce choroidal vascular proliferation and accelerate the progression of AMD to exudative AMD[30,33].

Our survey confirmed that sun exposure was another important risk factor for AMD, and this is consistent with some cross-sectional studies[34-36]. It is currently agreed that RPE cell damage is a key reason for the progression of AMD. In the past decades, extensive studies of ultraviolet and visible light, especially blue light, have caused damage to RPE cells. It has been confirmed that irradiation of RPE cells with ultraviolet A or B will cause its activity to be reduced, and blue light may even reduce its activity by nearly 40%[37]. Excessive exposure to sunlight increases blue light entering the eye and induces AMD[38].

In recent years, some scholars believe that diabetes is another important risk factor for AMD[39-41], but this view is still controversial. Choi *et al*[41] found that the prevalence of early AMD was high in patients with diabetes. However, Tomany *et al*[42] suggested that diabetes is associated with geographic atrophy but not with exudative AMD and early AMD. Our study found that there was a high prevalence of AMD in patients with diabetes, especially those with diabetes over 10y, but there was no clear correlation between fasting glucose and AMD. Our study did not detect glycosylated hemoglobin, or there may be some bias. Long-term elevation of blood glucose stimulates retinal epithelial cells to secrete vascular endothelial growth factor, which may lead to choroidal neovascularization.

The relationship between cataract surgery and AMD is not fully elucidated. A Meta-analysis pointed out that the history of cataract surgery is a strong risk factor for late AMD[8], but this correlation has not been suggested in randomized clinical

trials. Experts from Beijing Ophthalmology Research Center believe that cataract or cataract surgery has no correlation with early and late AMD[43]. Our survey suggests that the history of cataract surgery is a risk factor for AMD. The probable reason is the progression of macular degeneration caused by increased ultraviolet exposure after cataract surgery. However, cross-sectional study cannot exclude the missed diagnosis caused by the invisibility of the eyes of some patients before cataract surgery.

The relationship between blood lipid levels and the development of AMD is controversial[32,44-45]. Our survey found that the occurrence of AMD was positively correlated with serum total cholesterol. Therefore, in the prevention of AMD, it is recommended to adjust blood lipids to control the occurrence and development of AMD.

As with all population-based studies, an important limitation of our study is the lack of available data on diet, specifically of antioxidant intake, which is suggested risk factor for AMD[46].

The exact pathogenesis of AMD is not yet fully understood. There are many risk factors affecting AMD, and many related factors are controversial at present. We can actively conduct population-based AMD epidemiological surveys. It is helpful to investigate the risk factors of AMD and it is helpful to further study the pathogenesis of AMD to find an effective way to prevent, delay or treat AMD.

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