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Research Article

A Clinical Analysis of Age-Related Macular Degeneration in Qinghai Plateau

Aiqin Zhu[1*], Ling Li[2*], Xin Zhong[1], Guofeng Li[1], Yinlan Li[1], Xiangxi Guo[1], Junming Lou[1], Zhenghong Qing[2], Shengzheng Wu[1] and Jun Zhang[3]

Abstract:

Aim: To investigate the clinically estimated incidence and risk factors for age-related macular degeneration (AMD) in a various nationalities in Tibet and Qinghai plateau.

Methods: 185 AMD patients (288 eyes), aged 40 to 86 years and lived in Qinghai-Tibet plateau area (with a sea-level of 1800 m - 4300 m), were enrolled. All patients were assigned into four groups based on their nationalities. The Detached Angiography, Optical Coherence Tomography (OCT), Fundus Photography, Visual Acuity, Slit-Lamp Examination, Intraocular Pressure, Laboratory Blood Test were employed.

Results: The data showed that the Qinghai region's AMD patients in the 70 year old group are 43.25%, accounting for the largest proportion, while the 40 age group is 10.27%. AMD is significantly more prevalent in men than in women. In our 185 cases, the number of binocular cases is higher than that of the monocular. Dry AMD (56.25%) is higher than wet (43.75%). Blind and low vision patients constitute 9.03% and 28.47%, respectively. Vision loss in Tibetan patients is much higher than in Han patients (40.5% vs 28.6%). In the four different concentrations of hemoglobin, the 180 g/L group of AMD patients occupied 83 cases (44.86%). The vision damage is much more serious in exudative SMD than atrophic SMD determined by Fundus fluorescence angiography (FFA). The blood tests showed higher levels of triglycerides, red blood cells deposit, blood sugar, uric acid, and low density lipoprotein cholesterol (LDL-C) but lower levels of high density lipoprotein (HDL-C). Risk factors related to the plateau AMD may include: smoking, angiocardiopathy, hypertension, chronic obstructive pulmonary disease, and diabetes.

Conclusion: The chronic hypoxia environment may contribute to systemic changes of the body including retinal macular degeneration. Age, sex, smoking, particularly angiocardiopathy may be the main risk factors associated with AMD in the Qinghai-Tibetan Plateau.

Keywords

Age-related macular degeneration; Chronic hypoxia environment; Risk factors

*Corresponding authors: Aiqin Zhu and Ling Li, Institute of Geriatric, Qinghai Provincial Hospital, Xining -810007, P R China, Tel: 86-971-8066315; Fax: 86-971-8176273; E-mail: zhuaq@hotmail.com

Introduction

Age-related macular degeneration (AMD) is a major cause of irreversible vision loss in the elder population of European and American countries. Clinically, AMD has two types: dry AMD (atrophic) and wet AMD (Neovascular or exudative). 80-90% of individuals with AMD are dry AMD. It is characterized by drusen formation on the retina and geographic atrophy in local retinal pigment epithelium (RPE). Although wet AMD affects approximately 10-15% of individuals with AMD, it is the direct and major cause of severe vision loss from the disease due to retinal choroid neovascularization (CNV), macular hemorrhage or leakage of fluid into the RPE and sub-retinal spaces. AMD is a highly complex and multifactorial disease with demographic, environmental, and genetic risk factors including aging, smoking, diet and race [1]. Thus, the pathogenesis for AMD has yet to be completely understood. In China, AMD has become the third major cause of blindness. A few studies showed a high rate of wet AMD for peoples who lived in Qinghai-Tibet Plateau [2-5]. However, whether high plateau is a risk factor remains undetermined. In order to understand the characteristics of AMD in the plateau area, we collected and analyzed recent three-year's clinical data from AMD patients who were hospitalized in Qinghai Provincial Hospital and lived in high altitude regions (sea level is more than 1800 m) with various nationalities.

Objects and Methods

Clinical data

We collected 185 cases (total 288 eyes) of AMD patients from Qinghai Provincial People's Hospital, 59 cases of 80 eyes with cataracts, between January 2010 and October 2013 outpatient and hospitalization. These patients were from the Qinghai-Tibet plateau area (Qinghai Province, capital city Xining); an average elevation of 3100 meters (1800-4300 m). The average age of the patients is 68.79 ± 11.86 and the range is 40-86. The patients' nationalities include Tibetan, Han, Muslin, etc. The patients' occupations consist of workers, farmers, herdsmen, teachers, retirees, housewives, etc. All patients have received at least an elementary education (Table 1).

Methods

Multiple types of equipment and examinations were used throughout this experiment. These included retina detached angiography (HRA–II, Germany Heidelberg), Optical Coherence Tomography imaging scanner (OCT, model: SPECTRALIS, Heidelberg, Germany) and Fundus camera (Beijing Gaoyun technology co., LTD, Beijing, China). We analyzed patients' ophthalmological clinical data of visual acuity, intraocular pressure, slit-lamp examination, direct ophthalmoscope, fundus examination, fundus color photography, fundus fluorescein angiography, etc. To ensure a reliable inspection method and inspection results, all examinations were conducted by specially trained ophthalmologists. The epidemiological survey and questionnaires on the population sample size, lifestyle and disease were designed and conducted by the senior ophthalmologist of the Qinghai Provincial Hospital. The details included: (1) general demographic information: age, gender,

Table 1: AMD age distribution in plateau area.

Age(year)	40-	50-	60-	70-	≥80	Total
n	19	26	42	80	18	185
Proportion (%)	10.27	14.05	22.71	43.25	9.72	100

educational level, nationality, occupation, dietary habits, family life, place of residence and living conditions; (2) medical history: hypertension, diabetes, hyperlipidemia, cerebrovascular disease, coronary heart disease; (3) lifestyle and behavior factors: smoking, drinking alcohol; (4) vision, AMD family history.

AMD diagnosis and classification criteria

AMD clinical diagnosis were based on the early and the latest relevant criteria for age-related eye disease study (AREDS, nei.nih. gov), American Academy of Ophthalmology [6] and the Chinese Ophthalmological Society [7,8]. Exclusion criteria include (1) high degree myopia ≥6.0 D; (2) polypoidal choroidal vasculopathy; (3) Macular dystrophy syndrome; (4) Central serous chorioretinopathy; (5) Various types of vein occlusion; (6) Diabetic retinopathy; (7) Uveitis.

Laboratory method

10 ml of venous blood were collected from all AMD patients on an empty stomach (i.e. at least 12 h without eating solid or liquid meals). After using 5 ml of venous blood with ethylenediamine tetraacetic acid disodium salt (EDTA - Na2) anticoagulant, the red blood cells deposited (HCT) and hemoglobin (Hemochrome) were analyzed by using the Japanese Sysmex XT - 1800 automatic blood cell analyzer. The samples were centrifuged to separate the serum which was stored in -70°C until testing. The uric acid (UA), glucose (Glu), blood fat triglycerides (TG), cholesterol (TC), low density lipoprotein (LDL-C) and high-density lipoprotein (HDL-C), were tested using kit (Landau British company, UK).

Statistical methods

The demographic characteristics of AMD cases were described. The Chi-square test was performed by SPSS 16.0 software. P values< 0.05 were considered as statistically significant.

Results

General data investigation

In the 185 cases (288 eyes) of AMD patients, the group aged 70< is the largest. AMD tends to be more vulnerable to the senior population, and tends to affect both eyes. Binocular cases were significantly higher than monocular cases (111vs.74). Among the 185 cases, 45 cases had dry AMD, 28 cases had wet AMD and 38 cases had mixed dry and wet AMD. Of the total cases, 109 cases (58.92%) were men, and 76 cases (41.08%) were women. In the Dry AMD, 110 eyes were men, and 55 eyes were women. In the Wet AMD, 76 eyes were men, and 46 eyes were women (Table 2). The incidence in men was higher than in women, but there was no statistically significant difference (*P*>0.05) (Table 3). Visual acuity found in our AMD patients had a higher percentage of blindness and low vision: 26 blind eyes accounted for 9.03%; 82 low vision eyes accounted for 28.47%. The morbidity of blindness and vision loss in Tibetan patients was just below that of the Han, which was the highest.

The relationship with national, altitude, hemoglobin in plateau

The 185 patients with AMD come from five different nationalities, including Han, Tibetan, Muslin, Mongol, and Tu. Han (125/185, 67.57%) accounted for the largest; Tibetan patients(32/185, 17.3%) just below the Han was in second largest (Table 3). In terms of altitude, Xining Qinghai region (1800-2299 m, moderately high altitude) was the highest proportion (122 patients, 65.94%); Qinghai lake region (2300-3399 m, high altitude) was the second highest proportion (51 cases 27.57%). In Guoluo and Yushu regions of Qinghai province (above 3800 m), 12 patients with AMD accounted for 6.49% (Table 4). From the relationship between AMD and hemoglobin, hemoglobin AMD 180 g/L group was the highest hemochrome group among the four different concentration hemoglobin group (Table 5).

AMD with systemic diseases

AMD patients were often affiliated with systemic diseases such as high blood pressure, diabetes, coronary heart disease, chronic obstructive pulmonary disease (COPD), etc. Blood test results showed that the influence on AMD (from major to minor) are triglycerides, hematocrit (HCT), glucose (Glu), uric acid, low density lipoprotein cholesterol(LDL-C), total cholesterol(TC), and high density lipoprotein(HDL-C). 41 cases (22.16%) smokes, 35 cases (18.91%) drinks (Figures 1 and 2).

Macular lesion characteristics of AMD patients in plateau area

The morphological features of the different stages of lesions in retinal microcirculation and angiography by Fundus field analysis (FFA) technique showed that in the plateau dry AMD group, the

Table 2: AMD and gender in plateau area.

eyes	Male			Female		
	Dry	Wet	Total	Dry	Wet	Total
n	111	76	187	55	46	101
Proportion (%)	59.36	40.64	100	54.46	45.54	100

x^2=0.646, *P* >0.05

Table 3: Different nationalities AMD incidence.

Nationality	Han	Tibetan	Muslim	Mongol	Tu	Total
n	125	32	21	5	2	185
Proportion (%)	67.57	17.3	11.35	2.7	1.08	100

Table 4: Different high altitudes AMD incidence.

Altitute (m)	1800-	2300-	3400-	Total
N	122	51	12	185
Proportion (%)	65.95	27.57	6.48	100

Table 5: Different concentration hemoglobin AMD incidence.

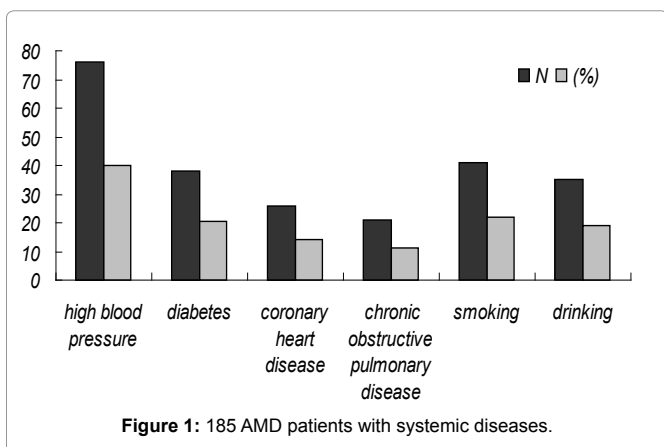| Hemochrome(mg/l)	100-	140-	180-	200-	Total
N	19	70	84	12	185
Proportion (%)	10.26	37.84	45.41	6.49	100

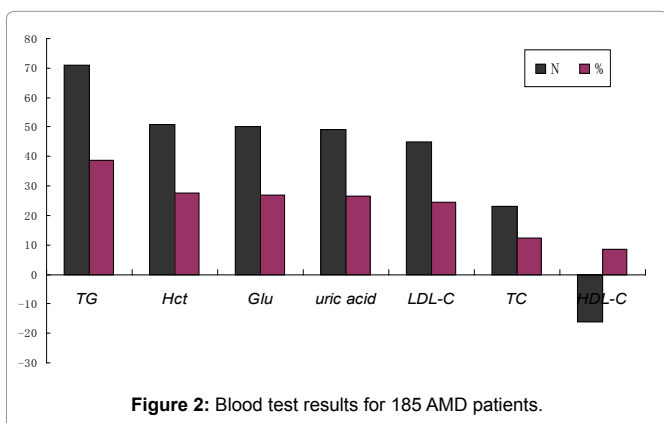**Figure 1:** 185 AMD patients with systemic diseases.

Figure 2: Blood test results for 185 AMD patients.

early lesions included choroid poor filling, accompanied by drusen and fluorescence macular, shade of pigment, drusen coloring. The late lesions included fluorescence spots progressively strengthened and leaked. In the wet AMD group, the early lesions included uneven drusen, window-like fluorescence spots, and the high fluorescence spot at the centre of the concave CNV boundary with dye leakage, fluorescence area extension, fluorescence covering bleeding area. In the late, macular presented large pale scar tissue (Figures 3 and 4). Figure 5 shows the different age groups and normal AMD by OCT. With the increase of age, the retina will gradually thinning, pigment on cortex will be uneven and retinal pigment epithelium will be serous detachment with macular center concave CNV

Discussion

AMD is the leading cause of senile severe vision loss. Despite much progress, the pathogenesis is still unclear. Most scholars believe that genetic, chronic light damage, nutritional deficiencies, poisoning, metabolism, ethnic, diet, immune system, etc may lead to retinal pigment epithelium cells and nerve retinal degeneration, causing irreversible vision loss [9,10]. AMD is currently one of the leading causes of blindness in the senior population of Europe and the United States [11]. Even though AMD has not yet become the leading cause of blindness in China, incidences of AMD have become our country's third largest, the harm along with China's aging of population is increasing gradually [12,13]. Qinghai is located in northeast of Qinghai-Tibet Plateau, latitude 36° 37', an average elevation of over 3,500 m, the annual average temperature in 2 to 9°C,annual sunshine at about 2,762 hours, continental climate of the plateau. The

characteristics of this region are low temperature, large temperature difference from day and night, long sunshine, strong solar radiation, and low oxygen partial pressure. At an altitude of 4,000 m, the oxygen partial pressure in the air is only 55 mmHg, at an altitude of 3000 m in the oxygen partial pressure is 67 mmHg in the air, at an altitude of 2,200 m in the oxygen partial pressure in the air is 77 mmHg. Qinghai is dry, windy, and cold, with huge temperature differences between each region, day and night. People living in these areas experience many environmental stresses, including chronic hypoxia, strong solar infrared and ultraviolet radiation, high altitude and relative isolation from the outside world. The unique environment of plateau has different effects on visual organs of human. Chinese scholars found that the plateau's low oxygen's main effect on retinal blood circulation, the change of the blood vessels, visible through fundus, results in the arterial spasm, intravenous expansion and bending, and early retinal hemorrhages performance [14]. Wu and Chen's study also showed that there was a higher AMD incidence in the high altitude areas of Tibet. Nevertheless, they thought the longer sunshine time, the stronger ground radiation may contribute to the pathogenesis of AMD [3,15,16]. AMD is the most common blinding eye disease for people over the age of 50. According to the statistics of people aged 50-65, morbidity was 11.6%, people aged over 75 had morbidity as high as 30% [17,18] which is similar to our case survey results. Regardless of nationality, its incidence is closely related to age. Our data on Qinghai region's younger AMD patients in the 40 age group is 10.27%, while the 70 year old group is 43.25%, accounting for the largest proportion. Our data also found that men were significantly more prevalent than
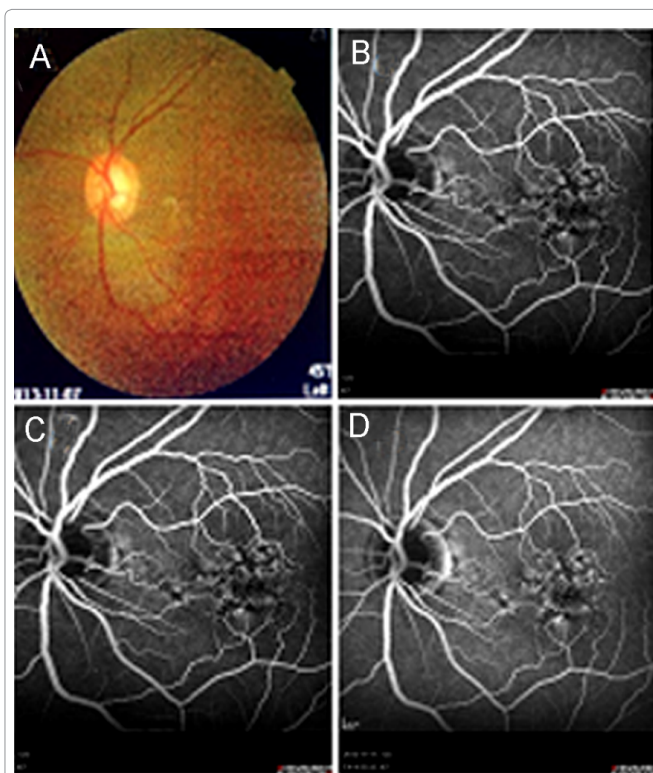

Figure 3: A female 62-year-old dry AMD patient had the left eye deformation more than 1 year. Drusen in the macular area can be observed by color fundus photographs (CFPs) (A); FFA examination results in early visible warts caused by uneven glass membrane window-like fluorescence defect (B); Medium-term for fluorescent spot gradually strengthened and leakage (C); Late stage for fluorescence spots gradually strengthened and leakage (D).
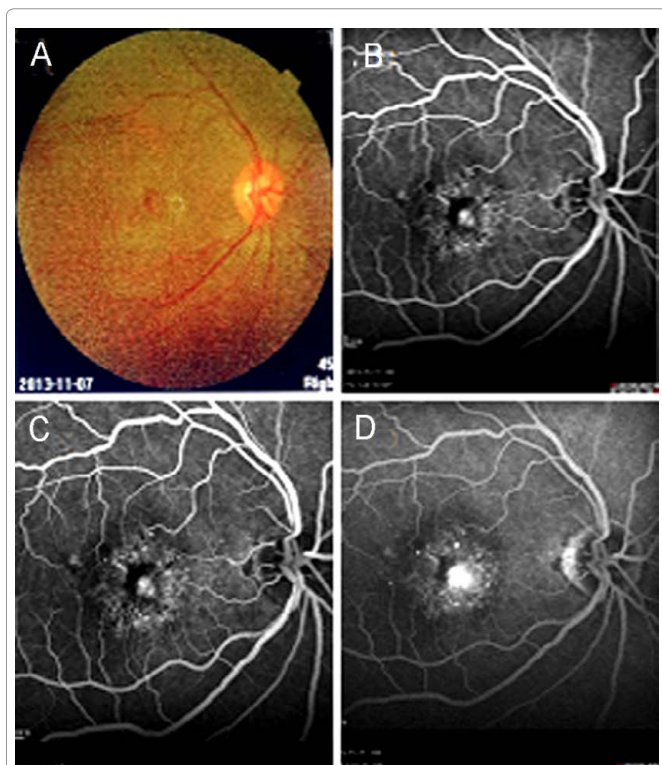
Figure 4: A female 56-year-old wet AMD patient has the right eye vision deformation more than 1 year. Retinal hemorrhage in the macular area by stove color photos (A); FFA examination results show early visible warts caused by uneven glass membrane window-like fluorescence spots, and the centre of high fluorescence spot at concave CNV boundary (B); bleeding keeps out fluorescence at the its temporal side and top edges (C); middle-late for fluorescence spots gradually strengthened and leaked (C,D).
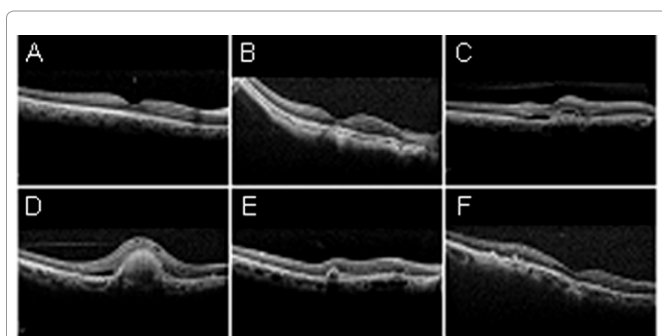
Figure 5: OCT images showing different age. Normal OCT (A); OCT for 45-year-old AMD patients visual cortex on retinal pigment is uneven (B); 56-year-old patient with AMD showing serious detachment with CNV(C; 67 age group AMD patients with macular center concave CNV (D); 78-year-old AMD patients with serious retinal pigment epithelium shallow (E); 88-year-old AMD patients having thinning of the retina, uneven pigment in the cortex (F).

women. This may be related to the male contact risk factors including: stronger sun radiation, longer possible outdoor work and more possible smoking. But our country census [19] there is no difference between men and women in the plain area. In our AMD185 case, binocular ratio is higher than that of monocular. Dry AMD (56.25%) is higher than wet AMD. Our Qinghai province results are the same as the other investigations from Henan Province of plain area the priority is dry AMD [20], but is different from Wu [2] and Chen's [4] reports that wet AMD is given priority in the plateau region.

This group of data found that the AMD incidence was affected by the remote locations, the undeveloped economy, isolated location, slow information dissemination, poor health condition, low education degrees, poor awareness of physicians and eye care. The ratio of in-patients in higher altitude areas is much lower than the lower altitude areas due to the larger number of farmers and herdsmen in higher altitude areas, who have less knowledge of eye diseases and are restricted to traditional ideals. In 4 different concentrations of hemoglobin, the 180 g/L group of AMD patients occupied 83 cases (44.86%) which may be related to the older population who have lived a longer time with erythrocytosis at the higher altitude and low oxygen environment. Thus this has resulted in a higher concentration of hemoglobin, higher blood viscosity, blood flow resistance and erythrocyte aggregation which led to micro thrombosis and the higher incidence in this group caused by fundus changes [21]. Han Chinese Group is the largest nationality, Tibetan patients in the second highest of our 185 cases AMD. The loss of vision in Tibetan patients was much higher than in Han patients. This may be related to the national quality, the different geographical conditions of life, and also the population distribution density of local residents.

Large quantities of evidence indicated that there were a large number of AMD risk factors, which include individual factors, systemic factors, environmental factors and genetic factors. Cardiovascular diseases such as various types of atherosclerosis and high blood pressure can increase the risk of AMD, leading to harden choroid, thicken the vessel wall, decrease inner diameter, increase blood flow resistance, decrease blood supply of eyes. These will then result in RPE lesions, separate cone and rod, induce the occurrence of AMD [22]. Diabetes is also a risk factor and is often complicated with cardiovascular disease. Keilhauer [23], on the other hand, showed that there was not a linkage between the pathogenesis of AMD and hyperlipidemia, myocardial infarction. In other systemic diseases, Klein [24] indicated emphysema was an independent risk factor out of smoking and age. Gout patients are a 2.48-fold increased risk of geographic atrophy (GA). Modest relationships between both increased the white blood cell count and emphysema and increased the 10-year incidence of lesions that defined early and late age-related maculopathy. Our data showed that there was a high proportion with high blood pressure, diabetes, cardiovascular disease, and chronic obstructive pulmonary disease (COPD) among the plateau AMD patients. The laboratory test results also showed that the levels of triglycerides, red blood cells deposit, blood sugar, uric acid, low density lipoprotein cholesterol (LDL-C) were higher than normal, but the high density lipoprotein (HDL-C) was lower than normal. Large qualities of risk factors may play a role in contributing to the pathogenesis of AMD such as lower plateau oxygen tension, diet of fewer vitamins, rich amounts of protein and lipid. The vision damage was much more serious in exudative SMD than atrophic SMD by FFA for retinal microcirculation and imaging examination. There were specific FFA manifestations in the different stages of lesions of retinal microcirculation. This is worthy of attention to the AMD problem in the plateau area.

In summary, Qinghai province is located in high altitude remote areas, where are poor economy, lower education levels, poor health condition and poor awareness of medical treatment which cause the patients to generally delay to the hospital. Most eye diseases have developed to the late stages, missing opportunities for treatment. The fundus diseases treatment has room for further improvement. The regular examination of fundus fluorescence angiography may be

valuable in finding early retinal neovascularization to prevent serious visual impairments.

Conflict of Interests

The authors declare they have no conflict of interests.

Acknowledgments

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Author Affiliation

[1]*Institute of Geriatric, Qinghai Provincial Hospital, Xining- 810007, China*
[2]*Department of Ophthalmology, Qinghai Provincial Hospital, Xining 810007, China*
[3]*Synaptic Physiology Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA*