Review Article

CLINICAL PRESENTATION AND RISK FACTORS OF AGE RELATED MACULAR DEGENERATION: A REVIEW.

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ABSTRACT

Background: Age-related macular degeneration (ARMD) is one of the age-related eye diseases (AREDs) in relation to low vision and blindness of great concern globally. With life expectancy on the increase, we expect to see more aged people. This will result in an increase in patients with Age-related Eye Diseases (AREDs).

Objective: The objective of this article was to identify the risk factors and forms of presentation of this disease.

Methods: Information for this review article was sourced from journal articles, Google Scholar, Google and Pubmed search engines. The search words included age-related macular degeneration, risk factors, clinical characteristics.

Results: Age-related macular degeneration represents a sizeable amount of retinal diseases globally. Risk factors associated with Age-Related Macular Degeneration include age (60 years and above), lifestyle (cigarette smoking and diet), refractive error (myopia) and the presence of lens opacities. Other factors such as genetics, systemic comorbidities (hypertension, diabetes mellitus and dyslipidaemia) have also been implicated. The presenting pattern is predominantly the early type. The clinical features are largely characterised by reduction in visual acuity, especially for the late type where it is more marked, the presence of retinal hyperpigmentation and hard drusen.

Conclusion: The clinical characteristics of ARMD, manifestations and predominant type show racial differences, the advanced form being more prevalent in Whites and the early forms in Blacks. Identification of risk factors for ARMD would help to reduce the risk of development or progression of this disease condition.

Key words: Clinical presentation, risk factors, age-related macular degeneration.

Introduction

Age-related macular degeneration (ARMD) is one of the age-related eye diseases (AREDs) in relation to low vision and blindness of great concern globally. It is a progressive neuroretinal degenerative disease in which patients advance from early and intermediate stages characterised by changes in pigment and drusen deposits to more advanced pathology, such as geographic

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atrophy (GA) and choroidal neovascularization (CNV).[1] It ranks third among the global causes of visual impairment with a blindness prevalence of 8.7%.[2] It commonly occurs in the sixth decade of life and is generally bilateral.[3] ARMD increases with age in men and women, but no significant sex differences in rates has been found.[4]

It is the leading cause of visual loss and blindness in Western countries.[3,5-8] In developing countries, there is paucity of data on the prevalence of this disease, possibly due to the non-availability of equipment needed to make an accurate diagnosis of this important cause of low vision and blindness in the aging population.[9]

Generally, two pathological forms of the disease have been identified, namely neovascular (wet ARMD) and atrophic. However, a third form has been documented, which is the indeterminate group.[2] The exact pathogenic mechanisms of ARMD are not completely understood. Precise clinical characterization of early lesions of ARMD and their progression over time can provide insight into the pathophysiology to guide research on treatments.[10-13] Treatment of ARMD ranges from careful observation, nutritional supplements, to laser therapy, photodynamic therapy, intravitreal injection of antivascular endothelial growth factor (anti VEGF) and surgical therapy. Current options for prevention are limited, but new treatments are being developed to preserve or restore vision in some patients with the wet form. Since life expectancy is increasing, we expect to see more aged people.[14] This will result in an increase in patients with Age-related Eye Diseases (AREDs).

The International Age-related Maculopathy Epidemiological Study Group[15] defines Age-related Maculopathy (ARM) as a degenerative disorder of the macular area, most often clinically apparent after 50 years of age, characterised by discrete whitish-yellowish spots identified as drusen, increased pigment or hyperpigmentation associated with drusen, sharply demarcated areas of depigmentation or hypopigmentation of the retinal pigment epithelium (RPE) and associated drusen. These result in progressive accumulation of debris under the retina. Visual acuity is not used to define the presence of ARM.

Early ARM is defined as the presence of drusen and RPE pigmentary abnormalities. Late ARM is similar to age-related macular degeneration (ARMD) and includes dry ARMD (geographic atrophy of the RPE in the absence of neovascular AMD) or neovascular AMD (RPE detachment, haemorrhages and / or scars, choroidal neovascular membrane).[15,16] It is the leading cause of blindness among people aged 55years and older in the United States of America (U.S.A.) and other western countries and was estimated to be responsible for 5% of global blindness in 2010.[17,18] Neovascular ARMD results in severe visual impairment if left untreated with an average loss of about four lines of visual acuity within two years of disease onset.[19]Visual impairment resulting from advanced ARMD significantly reduces quality of life and consumes more than fifty percent (50%) of eye care cost in the Medicare budget.[20]

Epidemiology

Age-related macular degeneration ranks third among the global causes of visual impairment with a blindness prevalence of 8.7%.[2] Many population and hospital-based studies of age-related macular degeneration have been reported around the world.[21-29] In Australia, the commonest cause of blindness (presenting visual acuity of less than 6/60, based on the guidelines for the study) is ARMD (48%), and the predicted numbers of Australians who will have low vision or blindness from ARMD will almost double over years 2000 – 2024.[30] Macular degeneration affects 1 in 7 Australians over the age of 50, with the incidence increasing with age.[12] In another Australian study (The Blue Mountains Eye Study) done to examine the prevalence of age related maculopathy (drusen and retinal pigmentary abnormalities) and end-stage age-related macular degeneration lesions (neovascular maculopathy or geographic atrophy) in a defined older Australian urban population, there was a marked age-related increase in all typical lesions of age-related

maculopathy.[12] End-stage age-related macular degeneration was present in 1.9% of the population, rising from 0% among people younger than 55 years of age to 18.5% among those 85 years of age or older.

In a clinical study done in England and Wales in the United Kingdom (UK), ARMD accounted for 42% of blindness in individuals aged 65 – 75 years.[31] This figure increased dramatically with age such that ARMD accounted for 75% of blindness in those aged 85 years and above.[31] Half of 30,000 people registered blind or partially sighted every year have macular degeneration.[32]

In the United States of America alone, where the population is approximately 312 million, the Eye Diseases Prevalence Research Group have estimated that more than 7.3 million people are affected by ARMD.[33] In another report, they further estimated that the number of advanced ARMD cases will reach almost 3million by 2020.[34]

In Asia, population-based studies have been done to estimate the prevalence of ARMD and comparisons made with the white population. A meta-analysis carried out to determine the prevalence of ARMD in Asians showed that pooled estimates of early and late ARMD in Asian populations aged 40 – 79 years were 6.8% (95% CI, 4.6% - 8.9%) and 0.56% (95% CI, 0.30% - 0.81%) respectively.[35] Another population-based study among one thousand four hundred and eighty six (1,486) residents of Hisayama town, Japan, to determine the prevalence of ARM in a representative older Japanese population showed the prevalence rate of drusen in both gender was 9.6%.[36] The prevalence of late ARMD was comparable to that in Western populations.[37-39] A population-based cross-sectional study by Cheung *et al*[40] to describe the prevalence and risk factors for ARMD in a multi-ethnic group among persons of Chinese, Indian and Malay ethnicities concluded that the prevalence of ARMD in the three ethnic groups studied was comparable with that observed in whites.

Very little is known about ARMD in African populations. There is a paucity of population-based studies and the majority of the few available are hospital based. In a population-based study in Kenya, East Africa, 100 clusters of 50 people aged 50 years or older were selected by probability-proportional-to-size sampling between 26 January 2007 and 11 November 2008. Age-related macular degeneration was found to be a significant contributor to visual impairment and blindness in the elderly. Early and late ARMD prevalence were 11.2% and 1.2% respectively, among participants graded on images.[41]

Studies from Nigeria have mainly been hospital-based. Abdulraheem *et al*[42] found that age-related macular degeneration was the fourth commonest cause of bilateral blindness with a prevalence of 8.1% in a five year review of elderly patients seen in the eye clinic of the University of Ilorin Teaching Hospital, in the North Central region of Nigeria. In Western Nigeria, Abiose[43] reported that age-related macular degeneration accounted for 25.9% of retinal diseases in Lagos (1.2% of all patients seen) in a study of five hundred and ninety five (595) new patients in the eye clinic of Lagos University Teaching Hospital thirty years ago (1976). Fafowora and Osuntokun[44] documented a prevalence of 3.4% for age-related macular degeneration and found that age-related macular degeneration represented a sizeable amount of retinal diseases even in rural communities. Onakpoya *et al*[45] found 13% of patients with vitreo-retinal disease in a five year review of the new patients seen in the eye clinic of Obafemi Awolowo University Teaching Hospital, Ile-Ife. ARMD was the most frequent macular disease with a prevalence of 13.7%. Oluleye *et al*[46] found that 35.6% of the patients had macular disease and ARMD accounted for 17.2% of all retinal diseases in a five year review of vitreo-retinal patients seen in the eye clinic of the University College Hospital, Ibadan. In the East, Nwosu[47] in a retrospective study conducted between 1997 and 2004 on seven thousand nine hundred and sixty six (7,966) new patients aged 50 years and above at the Guinness Eye Centre Onitsha, found that two hundred and fifty six patients had ARMD, an incidence of 3.2%. ARMD

was the main cause of blindness in 7.4% of the patients. Eze *et al*[48] found that vitreo-retinal disease accounted for 3.9% of which ARMD (third in the order) accounted for 10.7% in a four year review of new patients seen at the eye clinic of the University Teaching Hospital, Enugu. Macular degeneration accounted for 2.9% of blindness in the rainforest (south-west) region of Nigeria, as stated in the Nigerian National Blindness and Visual Impairment Survey.[49]

In the Mid-Western/South-South region, Ayanru[50] noted that macular degeneration was common among Nigerians with a prevalence of 2.2% in a study done in Benin City, thirty years ago (1976). In a review of ARMD in Benin City, Omoti[51] reported an incidence of 5% and for those over 50 years of age, 16.16%. Age-related macular degeneration was found to be the third leading cause of binocular blindness after cataract and glaucoma.[51] In a study to determine the pattern of retinal diseases in a tertiary hospital in Southern Nigeria by Uhumwangho *et al*[21], ARMD accounted for 15.0% of retinal cases seen and was noted to be the leading cause of bilateral blindness in the elderly (38.1%).

Classification

This is based on the International ARM Epidemiological Study Group.[15]

ARMD is classified as:

Early ARM

- Soft drusen> 63µm
- Areas of increased pigment or hyperpigmentation (in the outer retina or choroid) associated with drusen
- Areas of depigmentation of the RPE, most often more sharply demarcated than drusen, without any visibility of choroidal vessels, associated with drusen.

Late ARM = Age-related Macular Degeneration (AMD)

- Geographic atrophy ("dry" AMD)
- Any sharply delineated roughly round or oval area of hypopigmentation or depigmentation or apparent absence of the RPE in which choroidal vessels are more visible than in surrounding areas that must be at least 175µm in diameter.

- Neovascular AMD ("disciform", "exudative", or "wet" AMD)
- RPE detachment(s) which may be associated with neurosensory retinal detachment, associated with other forms of ARM.
- Sub-retinal or sub-RPE neovascular membrane(s)
- Epiretinal (with exclusion of idiopathic puckers), intraretinal, subretinal or sub-pigment epithelial scar / glial tissue or fibrin-like deposits.
- Subretinal haemorrhages that may be nearly black, bright red or whitish-yellow and that are not related to other retinal vascular disease.
- Hard exudates (lipids) within the macular area related to any of the above and not related to other retinal vascular disease.

DEFINITION OF TERMS

DRUSEN

Defined as tiny yellow or white accumulations of extracellular material that build up in Bruch's membrane. Drusen could be soft or hard.

Soft drusen: > 63 micrometres (µm) in diameter.

Hard drusen: Well defined and <63 micrometres (µm) in diameter.

RETINAL PIGMENTARY ABNORMALITIES

a) Retinal hypopigmentation: Defined as a discrete area of retinal pigment degeneration without visible choroidal vessels.

b) Retinal hyperpigmentation: Defined as presence of clumps of grey or black pigment beneath the retina.

EARLY AGE RELATED MACULOPATHY (ARM) Presence of one or more drusen≥ 125 µm (with or without pigmentary abnormalities) or

one or more drusen 63 - 124µm with pigmentary abnormalities in a 6000µm diameter grading grid centered on the fovea, in the absence of advanced AMD in either eye (geographic atrophy or neovascular AMD).

LATE AGE RELATED MACULOPATHY (AMD)

Tagged AMD by the International ARM group,[15] this includes:

a) Geographic atrophy: Disease area of retinal depigmentation characterized by sharp edges >175µm in diameter and visible choroidal vessels in the absence of exudative AMD.

b) Exudative / Neovascular AMD: Includes the presence of:

i. Serous haemorrhagic detachment of RPE of sensory retina.

ii. Sub-retinal or sub-pigment epithelial haemorrhage or sub-retinal fibrous scar.

iii. Photocoagulation scars from laser therapy for sub-retinal neovascular membrane.

iv. Choroidal neovascularization.

Risk factors

Many risk factors have been identified for ARMD and these include:

1. Age

Age has been implicated as the strongest risk factor for age related macular degeneration. It is a leading cause of visual loss in the elderly globally.[52-54] There is an increased preponderance of the disease as age increases, being more clinically apparent after 50 years of age, though data from the United Kingdom reflects individuals aged 65-75 years having age-related macular degeneration.[12,15,31] Data from three population-based studies namely the Blue Mountains Eye Study, Beaver Dam Eye Study and the Rotterdam Study show an increase in prevalence of ARMD from 0 – 2% in patients aged 55 – 64 years to about 13% in patients over 85 years.[55] Findings from the Eastern and Mid-Western parts of Nigeria show an increase in the occurrence of this disease with advancing age.[47,51]

2. Lifestyle

a. Tobacco smoking

Cigarette smoking is a well-established risk factor for the development of age related macular degeneration.[56-59] It is a major modifiable risk factor for the development of age-related macular degeneration. Studies have shown that those who smoke are three times at risk of developing macular degeneration.[55] Smokers may develop macular degeneration about ten years earlier than non-smokers and there is a dose-response relationship between pack years of smoking and the development of ARMD.[57,60-62] A pack year reflects the lifetime exposure to tobacco by an individual and is expressed as a numerical value. It is calculated by multiplying the number of years an individual has smoked cigarettes by the number of packs of cigarettes smoked per day.[60]Several studies have investigated and confirmed this dose-response relationship. The Rotterdam and POLA (Pathologies Oculaires Liées à l'Age) studies showed increased risk of neovascular ARMD in individuals who had smoked 10 pack-years or more.[63,64] The Physicians' Health Study and the Nurses' Health Study found a two-fold higher risk of ARMD in individuals who had smoked more than 25 cigarettes per day.[65,66] The Beaver Dam Offspring Study confirmed that smoking 11 pack-years or more was associated with the presence of early ARMD.[67] Despite cessation of smoking, evidence shows that the risk of neovascular ARMD persists in ex-smokers of up to 20years, as confirmed by The Rotterdam and POLA studies.[63,64] Smoking has been implicated in the reduction of serum antioxidant levels which is a plausible mechanism by which age-related macular degeneration results in smokers.[68] Though smoking has been confirmed to be strongly associated with ARMD, some studies

found no association or only a very weak link between them.[69-74] West *et al*[69] found an insignificant reduced risk of ARMD in those who had ever smoked cigarettes, in a small cross-sectional study, and Blumenkranz *et al*[70] found a small insignificant increase among current smokers in a small case–control study. A large French case–control study found only a weak and insignificant association between ARMD with previous and current smoking.[71] Although the Beaver Dam Eye Study found a strong association between smoking and neovascular ARMD,[72] the association at the 5- and 10-year follow-up examinations was weaker.[73,74]

b. Alcohol intake

Although the pathophysiology of ARMD is not fully understood, some of the current theories on aetiology could implicate alcohol in their mechanisms of action. Alcohol is a known neurotoxin that can cause oxidative brain damage and, hence, it is logical that the retina could be similarly affected.[75,76] Two cross-sectional and three incidence studies found an association between alcohol consumption and risk of ARMD.[77-81] These were population-based studies which showed that heavy consumption of alcohol (> 5 drinks per session) increased the incidence of late ARMD. Beer drinking was associated with an increased risk of advanced ARMD but wine drinking was shown to be protective to the retinal pigment. In a prospective population-based study in Beaver Dam, heavy drinking (four or more drinks daily) at baseline was related to the 15-year cumulative incidence of pure geographic atrophy in men (odds ratio: 9.2, 95% confidence interval: 1.7-51.2). There were no consistent associations with the amount of beer, wine or liquor consumption and the incidence or progression of ARMD.[82] No association was found between overall or specific alcohol consumption and development of early ARMD or dry or wet late ARMD in the Rotterdam Study.[83] Cross-sectional analyses of the results of The Blue Mountains Eye Study[84] found no association between ARMD and overall alcohol intake and more specifically beer consumption; however, consumption of spirits was associated with the presence of early ARMD.

c. Diet and nutrition

Diet is emerging as a potentially modifiable risk factor for ARMD.[85-88] Research suggests that diet could influence the risk of ARMD, but the associations found have not been consistent across studies.[89-91] Diet high in trans-fat, and red meat, have been associated with an increased risk of ARMD,[86,92,93] whereas higher intakes of fish have been associated with a lower risk of ARMD.[91,94] Dietary pattern rather than specific food items have been implicated. Amirul *et al*[95] reported that a diet characterised by frequent consumption of boiled rice, muesli, fish (not fried), chicken (not fried), and a variety of vegetables and avoidance of white bread was associated with a lower prevalence of advanced ARMD, whereas a diet characterised by a pattern of eating red and processed meats and fried foods was associated with a higher prevalence of advanced ARMD. Evidence is continuing to mount that the choices we make about food we consume may play a role in contributing to the risk of developing ARMD.[95]

d. Obesity

Body Mass Index (BMI) calculated as weight in kilogrammes divided by height in metres squared, a measure of obesity, has been implicated as a risk factor for ARMD. In a hospital – based study conducted in Boston, higher BMI was shown to increase the risk of progression to advanced form of ARMD.[96] Relative risk (RR) was 2.35 (95% CI, 1.27 – 4.34) for a BMI of at least 30 and 2.32 (95% CI, 1.32 – 4.07) for a BMI of 25 – 29. Increased physical activity tended to be associated with a reduced rate of progression of ARMD (25% reduction for exercising 3 times weekly versus none, P = 0.05 – P = 0.07).

Another study showed that the incidence of visually significant dry ARMD was lowest in men with normal BMI, but no significant relationship of BMI and neovascular ARMD could be proven due to the few number of cases analysed in the

study.[97] The Beaver Dam Eye Study[98] examined the relationship between exercise and ARMD, concluding that walking at least 12 blocks a day decreased the incidence of wet ARMD by 30% over 15 years (OR 0.7, 95% CI 0.6 to 0.97). An active lifestyle (regular activity ≥ 3times weekly) decreased the risk of exudative ARMD (OR 0.3, 95% CI 0.1 – 0.7) compared with individuals with a sedentary lifestyle.[98] In general, reported findings suggest an increased risk of ARMD with increasing BMI and abdominal obesity.[99-101]

3. Ocular

a. Refractive status

A number of studies have reported an increased risk of ARMD associated with hyperopia.[102-107] Statistically significant associations were demonstrated between senile macular degeneration and hyperopia in a case – control study carried out in Baltimore, United States of America.[102] Sandberg et al[103] showed that patients with a refractive error of ≥ +0.75 D were more likely to have neovascular ARMD compared with patients with other refractive errors (odds ratio, 2.40; 95% confidence interval, 1.53-3.78; P < 0.001). Hyperopia was the most significant risk factor for ARMD in a study from North India.[107] Studies from Australia confirmed an association between hyperopia and AMD.[105,106]

The Eye Disease Case-Control Study found that persons with hyperopia had a slightly higher risk of neovascular AMD, but the association did not remain statistically significant after multivariate modelling.[108] One caveat in the interpretation of findings in these case-control studies is that because the controls were recruited from ophthalmology clinics, the control groups may be enriched in the proportion of myopes compared with the general population.[108]

b. Iris colour

Evidence is inconsistent for an association between iris colour and development of ARMD, but a plausible explanation is that the lower risk for ARMD among subjects with darker iris colour may be due to the fact that these individuals have more tissue melanin. This increased pigmentation may provide some protection to the retina from exposure to sunlight, reducing direct photo-oxidative damage and thus reducing the risk of ARMD. Despite this theoretic protective effect, iris colour has not consistently been associated with ARMD. Weiter *et al*[109] found that 76% of 650 patients with ARMD had light irides compared with 40% of 363 controls (p = 0.0001). In contrast, the Beaver Dam Eye Study found an inconsistent relationship between iris colour and 10-year incidence of drusen and pigmentary abnormalities.[110] The reasons for these disparities are not clear.

c. Macular pigment

Macular pigment is composed of two carotenoids, lutein and zeaxanthin, which are solely of dietary origin and which are found in a wide variety of green leafy plants such as spinach and kale and in some animal products such as egg yolk.[111] In the Age-related Eye Disease Study (AREDS), a higher dietary intake of lutein and zeaxanthin, measured using a self-administered food frequency questionnaire was associated with a statistically lower risk of developing advanced ARMD compared to having a lower intake.[112]

4. Systemic morbidities

a. Hypertension

Hypertension plausibly increases the risk of ARMD due to its effects on the choroidal circulation.[113] Some large population-based studies have shown a small and consistent association between ARMD and systemic hypertension. Kahn *et al*[114], using data from the Framingham Heart and Eye Studies found a positive association between the presence of ARMD and higher levels of diastolic blood pressure measured many years before eye examination. Sperduto and Hiller[115], using data from the Framingham Heart and Eye Studies, found the age and sex adjusted relative risk for any ARMD was 1.18 (95% CI, 1.01 – 1.37), for persons diagnosed with hypertension 25 years before eye examination and 1.04 (95% CI, 0.96 – 1.23) for persons with hypertension at the time of the eye examination, when compared with those

without hypertension. Other population-based cross-sectional studies detected no association between hypertension and ARMD, including the Blue Mountains Eye Study, Atherosclerosis Risk in Community Study and Andhra Pradesh Eye Disease Study.[116-118]

b. Diabetes mellitus

Many studies have investigated the relationship between diabetes mellitus and ARMD but few studies have found any link.[119] The Blue Mountains Eye Study found geographic atrophy to be significantly associated with diabetes (OR, 4.0; 95% CI, 1.6 – 10.3), but no association was found with either neovascular ARMD (OR, 1.2; 95% CI, 0.4 – 3.5) or early ARMD (OR, 1.0; 95% CI, 0.5 – 1.8). There was also no association found between impaired fasting glucose and ARMD in the Blue Mountains Eye Study and the Atherosclerosis Risk in Communities Study.[117,120]Choi *et al*[121] in a population-based study of 3008 participants aged 50 – 87 years found a significant association between diabetes mellitus and early age related macular degeneration (OR 1.87; 95% CI, 1.07 – 3.25). The mechanism is by altering the haemodynamics, increasing oxidative stress, with resultant accumulation of advanced glycation end-products.[122]

c. Hyperlipidaemia

Dietary fat intake, particularly intake of saturated fat and cholesterol has been suggested to be associated with an increased risk for atherosclerosis, thus increasing the risk for ARMD. The Eye Disease Case- Control Study[123] found that individuals with mid-range (4.889 – 6.748 mmol/L) and high (> 6.748mmol/L) total cholesterol levels compared with those with low levels (< 4.889mmol/L) had OR for neovascular ARMD of 2.2 (95% CI, 1.3 – 3.4) and 4.1 (95% CI, 2.3 – 7.3), respectively, after controlling for other factors. A slight but not statistically significant increased risk of neovascular ARMD was seen with increasing levels of serum triglycerides in the same study. Several other studies including the Rotterdam study, Blue Mountains Eye Study and Atherosclerosis Risk in Communities Study did not find any association between serum cholesterol and HDL cholesterol with AMD.[116,117,124] The Beaver Dam Eye Study and Blue Mountains Eye Study found no association between the use of lipid-lowering agents and the risk of developing ARMD.[120]

5. Genetic

A family history of ARMD is a risk factor for ARMD. In 2005 it was established that a mutation in a key regulator of the complement pathway: complement factor H (CFH) located on chromosome 1q31 is strongly associated with a risk of ARMD.[125,126] The Y402H polymorphism in this gene has a minor allele frequency of 40% and is highly associated with AMD.[126] Other genes with sequence variants established in all studies related to genetics and AMD include LOC 387715/PRSS 11 and BF/C2 protective variants. Some other variations have been reported to be associated with an increase in the risk of ARMD, but minimal support for these associations exist.

6. Others

a. Sunlight

It has been hypothesized that sun exposure is a risk factor for ARMD.[127-129] Light exposure, specifically blue light, bright sunlight, and ultraviolet (UV) radiation, has been implicated in photochemical oxidative damage and light-induced apoptosis of the RPE cells.[130,131]

b. Gender

Studies have reported a higher prevalence of ARMD in women, but much of this increased risk can be attributed to increased longevity in women.[74] In the Blue Mountains Eye Study[132] conducted in Sydney, Australia, women had higher prevalence of ARMD than men although no significant statistical difference was observed.

c. Social class

Studies have suggested that increasing years of education are associated with a decreased risk of ARMD but no strong associations have been

observed, hence the unlikelihood that social class would impact on the incidence of ARMD.[133,134]

d. Race

Age-related macular degeneration has been shown to have a racial predilection. A cross – sectional population-based study in East Baltimore conducted among blacks and whites identified drusen in both groups, large drusen (>125µm) occurring more frequently among older whites over 70years of age (15% versus 9%).[135] Pigmentary abnormalities were found to be more prevalent among the white population (7.9% versus 0.4%). Age-related macular degeneration had a prevalence rate of 2.1% among the white population over 70years of age with no ARMD detected in black subjects in this group.

In a multi-ethnic study of atherosclerosis among four racial ethnic groups (white, black, Hispanic and Chinese), the prevalence of ARMD was lower in blacks compared with whites (2.4% versus 5.4%).[136] White persons are generally more likely than black persons to have medium or large drusen, focal pigment abnormalities, and advanced ARMD. More severe forms of age-related maculopathy are more prevalent in older whites.[135]

e. Cataract and cataract surgery

It is thought that both ARMD and cataract result from accumulation of oxidative damage in the form of reactive oxygen species, from both internal sources (mitochondria) and external sources (sunlight).[137] A meta-analysis found that cataract surgery was associated with late ARMD with an odds risk ratio from pooled prospective studies of 3.05 (95% confidence intervals 2.05 - 4.55).[138] The Beaver Dam Eye Study was included in that meta-analysis, but has since published 15 year results, finding that cataract surgery is associated with increased ARMD risk, after correcting for other risk factors including complement factor H and age-related maculopathy susceptibility 2 (ARMS2) risk alleles.[139] The risk was greatest if surgery had been performed more than five years previously rather than less than five years from the study time-point.

Conclusion

The clinical characteristics of ARMD, manifestations and predominant type show racial and environmental differences. Identification of risk factors for ARMD would help to reduce the risk of development or progression of this disease condition.

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