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Age Related Macular Degeneration:A Systematic Review

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Abstract

Aim: To conduct a systematic review on Age related Macular degeneration

Objective:

To conduct a systematic review on age related Macular degeneration in order to make people aware of the risk of this degenerative disorder if gone untreated.

Background:

Age-related macular degeneration, often called AMD or ARMD, is the leading cause of vision loss and blindness .It usually affects the older population mainly those who are 65 years and older. It is the degeneration of the macula, which is the part of the retina responsible for the sharp, central vision needed to read or drive. Because the macula primarily is affected in AMD, central vision loss may occur. There are mainly two types of AMD the Wet form and the Dry form. The dry form is more common than the wet form, with about 85 to 90 percent of AMD patients diagnosed with dry AMD. The wet form of the disease usually leads to more serious vision loss.

Reason:

This systematic review is mainly done to create awareness on Age related macular degeneration which may be a leading cause of vision loss in aged people

Keywords- awareness, central vision, Elderly, Macular Degeneration, vision loss

INTRODUCTION

Age-related changes affect all structures of the eye, and while age-related changes may influence the quality of vision, it is important to distinguish age-related physiological changes from pathological changes. (1)

Age-related macular degeneration (AMD or ARMD), is a medical condition which may result in blurred or no vision in the center of the visual field.(2) Early on there are often no symptoms. Over time, however, some people experience a gradual worsening of vision that may affect one or both eyes. While it does not result in complete blindness, loss of central vision can make it hard to recognize faces, drive, read, or perform other activities of daily life. (2)

Macular degeneration typically occurs in older people. The prevalence of visual loss increases substantially after 60 years of age and poor vision is the second most prevalent physical disability in older people(1). Genetic factors and smoking also play a role. It is due to damage to the macula of the retina. Diagnosis is by a complete eye exam. The severity is divided into early, intermediate, and late types (2).The late type is additionally divided into "dry" and "wet" forms with the dry form predominantly being 90% of cases(3). Antioxidant vitamins and minerals do not appear to be useful for prevention (4).There is no cure or treatment that returns vision already lost. In the wet form, anti-VEGF medication injected into the eye or less commonly laser coagulation or photodynamic therapy may slow worsening (2).

In 2010 it affected 23.5 million people globally (6). In 2013 moderate to severe disease affected 13.4 million and it is the fourth most common cause of blindness after cataracts, preterm birth, and glaucoma (7)

AGE RELATED MACULAR DEGENERATION:

Human retina undergoes changes as part of the natural course of aging, resulting in the appearance of ophthalmoscopically visible focal yellow deposition of acellular, polymorphous debris called drusen between the retinal pigment epithelium and Bruch's membrane.

AMD patients display a broad spectrum of clinical characteristic based upon drusen size and AMD pigmentary abnormalities, both hypo pigmentation and hyper pigmentation (8).

The Macula

The macula is made up of millions of light-sensing cells that provide sharp, central vision. It is the most sensitive part of the retina, which is located at the back of the eye. The retina turns light into electrical signals and then sends these electrical signals through the optic nerve to the brain, where they are translated into the images we see. The progressive destruction of the macula is a disease known as macular degeneration and can sometimes lead to the creation of a macular hole. Macular holes are rarely caused by trauma, but if a severe blow is delivered it can burst the blood vessels going to the macula, destroying it (30).

When the macula is damaged, the center of your field of view may appear blurry, distorted, or dark (31, 32).

PATHOGENESIS OF AGE RELATED MACULAR DEGENERATION

The molecular pathways leading to age related macular degeneration remain to be elucidated. The retina and its pigmented epithelium are unique among body tissues in their constant exposure to light energy and high oxygen concentrations, both of which are potent sources of free radicals (9).

The photoreceptor-RPE-Bruch's membrane-choroid complex is a site of chronic oxidative damage that is most pronounced in the macula .This damage incites inflammation, mediated at least in part By complement activation, at the level of RPE-Bruch's membrane-choroid. Patients with mutations in components of the complement system are less able to modulate the inflammatory response, resulting in excessive cellular damage and accumulation of extracellular debris (10).

Accumulation of abnormal extracellular material (including membranous debris, oxidized molecules, extracellular matrix molecules, and components of the complement system) is thus a sign of chronic inflammatory damage, is manifest in part as drusen and pigmentary abnormalities, and fosters the development of the late squeal of AMD in susceptible individuals (10)

SIGNS AND SYMPTOMS

In early stages, age-related macular degeneration may not have symptoms and may be unrecognized until it progresses or affects both eyes. The first sign of macular degeneration is usually distortion of straight lines. This may progress to a gradual loss of central vision.

Macular degeneration by itself will not lead to total blindness. For that matter, only a very small number of people with visual impairment are totally blind. In almost all cases, some vision remains, mainly peripheral. Other complicating conditions may possibly lead to such an acute condition (severe stroke or trauma, untreated glaucoma, etc.), but few macular degeneration patients experience total visual loss (12).

The loss of central vision profoundly affects visual functioning. It is quite difficult, for example, to read without central vision. Pictures that attempt to depict the central visual loss of macular degeneration with a black spot do not really do justice to the devastating nature of the visual loss (47).

RISK FACTORS IN AMD

AMD is a multifactorial disease, typically caused by many genetic variants, each with modest effect on the risk and also influenced by non-genetic/environmental factors, such as diet and smoking (11). Long-term epidemiological studies have identified valuable information on the prevalence, incidences, natural history and associated risk factors of AMD (13, 14)

Age is one of the most important deciding factors in AMD. It is due to this that the main progression of AMD is decided.

Smoking tobacco increases the risk of AMD by two to three times that of someone who has never smoked. Cigarette smoking is likely to have toxic effects on the retina (15).

One of the other contributing risk factors was found to be elevated pulse pressure (PP) systolic BP minus diastolic BP) was significantly associated with an increased risk of late AMD (16).

Elevated cholesterol may increase the risk of AMD(17) Consuming high amounts of certain fats including saturated fats, trans fats and omega-6 fatty acids likely contributes to AMD(19).Abdominal obesity is a risk factor, especially among men (18) also over research it was found to be that high-energy visible light may contribute to AMD(20 ,21)

A 10-year longitudinal study, Multi-ethnic Study of Atherosclerosis (MESA) examined four racial/ethnic groups and reported lower prevalence of AMD in blacks than in whites with overall prevalence varying from 2.4% in African Americans, 4.2% in Hispanics, 4.6% in Chinese compared with 5.4% in whites (22).

INVOLVEMENT OF GENETICS

Genetics being involved in AMD is one of the main risk factor in AMD. Genetic contribution to the development of AMD has been established over the years through familial aggregation studies, twin studies, and segregation analyses (23).

In fact, instead of having a single contributory gene, there are multiple genes of variable effects that seem to be involved turning the issue of genetics of AMD a complex one (24): AMD involves environmental factors and varying susceptibilities to these external factors based upon different genetic backgrounds (25)

The genetic component of the disease has been suspected from family, twin and sibling studies. According to several family studies, patients with a family history of AMD have an increased risk for developing AMD (26, 27). Dissection of the genetic background of AMD has undergone tremendous progress in the last 2 years (24)

TYPES IN AMD

There are two main types of AMD that affect people and they are mainly the dry and wet age related macular degeneration. (28)

DRY AMD

Dry AMD begins with characteristic yellow deposits (drusen) in the macula, between the retinal pigment epithelium and the underlying choroid. Most people with these early changes (referred to as age-related maculopathy) still have good vision (47).

A few small drusen may not cause changes in vision; however, as they grow in size and increase in number, they may lead to a dimming or distortion of vision that people find most noticeable when they read. In more advanced stages of dry macular degeneration, there is also a thinning of the light-sensitive layer of cells in the macula leading to atrophy, or tissue death. In the atrophic form of dry macular degeneration, patients may have blind spots in the center of their vision. In the advanced stages, patients lose central vision (28) .The dry (atrophic) type affects approximately 80-90% of individuals with AMD (29).

WET AMD

The wet AMD also most commonly known as Neovascular or exudative AMD, the "wet" form of advanced AMD, causes vision loss due to abnormal blood vessel growth (choroidal neovascularization) in the choriocapillaris, through Bruch's membrane (48).

These blood vessels leak blood and fluid into the retina, causing distortion of vision that makes straight lines look

wavy, as well as blind spots and loss of central vision. These abnormal blood vessels and their bleeding eventually form a scar, leading to permanent loss of central vision (28) The wet/neovascular type affects approximately 10-15% of individuals with age-related macular degeneration, but accounts for approximately 90% of all cases of severe vision loss from the disease (29)

DIAGNOSIS

Diagnosis of age-related macular degeneration rests on signs in the macula, irrespective of visual acuity (49). Age-related macular degeneration can be detected in a routine eye exam. One of the most common early signs of macular degeneration is the presence of drusen -- tiny yellow deposits under the retina (28).

One of the main ways and tests which are performed in order to diagnose AMD are:

- **Amsler grid.** An eye care professional may also ask a patient to look at an Amsler grid. Changes in their central vision may cause the lines in the grid to disappear or appear wavy, a sign of AMD. This diagnostic test is one of the first tests done to see if the patient suffers from AMD.
- **Visual acuity test.** This eye chart measures how well a person sees at distances.
- **Dilated eye exam**. An eye care professional place drops in the persons eyes to widen or dilate the pupils. This provides a better view of the back of the eye. Using a special magnifying lens, he or she then looks at the retina and optic nerve for signs of AMD and other eye problems.
- **Fluorescein angiogram**. In this test, which is performed by an ophthalmologist, a fluorescent dye is injected into the patients arm. Pictures are taken as the dye passes through the blood vessels in their eye. This makes it possible to see leaking blood vessels, which occur in a severe, rapidly progressive type of AMD (see below). In rare cases, complications to the injection can arise, from nausea to more severe allergic reactions.
- **Optical coherence tomography.**OCT is similar to ultrasound except that it uses light waves, and can achieve very high-resolution images of any tissues that can be penetrated by light—such as the eyes. After the patient's eyes are dilated, they'll be asked to place their head on a chin rest and hold still for several seconds while the images are obtained. The light beam is painless (31, 32).

TREATMENT

With limited treatment option available, preventing the development and retarding the disease progression to minimize the vision loss remain high priorities in AMD management (8).

It was also seen that Dry AMD had No medical or surgical treatment is available for this condition. And Wet AMD can be treated with laser coagulation, and more commonly with medication that stops and sometimes reverses the growth of blood vessels (37,38).There is strong evidence that laser coagulation will result in the disappearance of drusens but does not affect choroidal neovascularisation (39).

Based on the severity or the stage of AMD it is mainly seen as 3 different stages:

1. **Early AMD**
   Currently, no treatment exists for early AMD, which in many people shows no symptoms or loss of vision (40).
2. **Intermediate and late AMD**
   Researchers at the National Eye Institute tested whether taking nutritional supplements could protect against AMD in the Age-Related Eye Disease Studies (AREDS1 and AREDS2). They found that daily intake of certain high-dose vitamins and minerals can slow progression of the disease in people who have intermediate AMD, and those who have late AMD in one eye.

Supplements may slow down the worsening of AMD (33). There is no enough evidence to determine if statins have a role in preventing or slowing the progression of AMD(34) Antiangiogenic steroids such as anecortave acetate and triamcinolone acetonide have shown no evidence in preventing visual loss in people with neovascular AMD(35)

AREDS1

The AREDS1 established that antioxidant vitamin and mineral supplementation (AREDS formulation) consisting of β-carotene (15mg), vitamins C (500 mg) and E (400 IU), and zinc (as zinc oxide 80 mg), along with copper (as cupric oxide 2mg) slowed progression of AMD in individuals at high risk of developing advanced AMD (36).

AREDS 2

AREDS2 showed that adding omega-3 fatty acids to the AREDS supplements were neither beneficial nor harmful (43). Adding lutein/zeaxanthin to the AREDS formulation resulted in additional beneficial effect of about 20% beyond the effects of AREDS formulation in reducing the risk of progressing to advanced AMD. Furthermore, beta-carotene was associated with an increased risk of lung cancer, mostly in former smokers (41)

A number of manufacturers offer nutritional supplements that were formulated based on these studies. The label may refer to "AREDS" or "AREDS2."

People with intermediate or late AMD, might benefit from taking such supplements.

AREDS formulation is not a cure. It does not help people with early AMD, and will not restore vision already lost from AMD. But it may delay the onset of late AMD. It also may help slow vision loss in people who already have late AMD (31, 32, 40).

Advanced Neovascular AMD

Neovascular AMD typically results in severe vision loss.

- **Injections**. One option to slow the progression of neovascular AMD is to inject drugs into the eye. With neovascular AMD, abnormally high levels of vascular endothelial growth factor (VEGF) are secreted in your eyes. VEGF is a protein that promotes the growth of new abnormal blood vessels. Anti-VEGF injection therapy blocks this growth
- **Photodynamic therapy**. This technique involves laser treatment of select areas of the retina. First, a drug

called verteporfin will be injected into a vein in the patient's arm. The drug travels through the blood vessels in the body, and is absorbed by new, growing blood vessels. The eye care professional then shines a laser beam into their eye to activate the drug in the new abnormal blood vessels, while sparing normal ones. Once activated, the drug closes off the new blood vessels, slows their growth, and slows the rate of vision loss. This procedure is less common than anti-VEGF injections, and is often used in combination with them for specific types of neovascular AMD.

- **Laser surgery**. Laser surgery for treating AMD though this is less common than other treatments. It involves aiming an intense "hot" laser at the abnormal blood vessels in the patient's eyes to destroy them. This treatment is more likely to be used when blood vessel growth is limited to a compact area in their eye, away from the center of the macula that can be easily targeted with the laser. Even so, laser treatment also may destroy some surrounding healthy tissue. This often results in a small blind spot where the laser has scarred the retina. In some cases, vision immediately after the surgery may be worse than it was before. But the surgery may also help prevent more severe vision loss from occurring years later (31, 32, 40).

Stem cell transplant

Cell based therapies using bone marrow stem cells as well as Retinal pigment epithelial transplantation is being studied (42) .Recent advancements within the field of stem cell research in the United States have led to the first human embryonic stem cell trial for dry AMD, which reports positive results (43).

PREVENTION

Although there's no treatment that can cure age-related macular degeneration (AMD), there are steps that may keep it from getting worse.

Research into the prevention of age related macular degeneration has focused on risk factors that exacerbate oxidative stress or interventions that ameliorate their effects, such as supplementation with antioxidant vitamins, particularly the macular carotenoids lutein and zeaxanthin. Stopping cigarette smoking is recommended since its adverse association with late age related macular degeneration is unequivocal (9).

It is also seen that AMD occurs less often in people who exercise, avoid smoking, and eat nutritious foods including green leafy vegetables and fish. If a person already has AMD, adopting some of these habits may help keep their vision longer (40).

Regular eye exams may help a person find out if they are at risk for AMD or, if they have AMD, may detect it early. Early detection can sometimes delay loss of vision.

People who smoke may be twice more likely to develop AMD than those who don't smoke. Even after they stop smoking, this increased risk may persist for many years (44).

Regular exercise, and staying at a healthy weight, these choices may lower a person's risk of getting AMD (45).

In people who already have moderate AMD, certain vitamins have been shown to help delay the onset of advanced AMD and/or help prevent further vision loss.

- Eating fish, a good source of omega-3 fatty acids, may lower a person's chances of getting wet AMD
- Limit harmful fats. Too much saturated fat and cholesterol in diet may increase the risk that AMD will get worse (44).

CONCLUSION

From this research we can hereby see that ARMD remains a significant public health concern and important cause of blindness in the elderly. Recent research has focused on the genetic factors responsible for the pathogenesis of ARMD (46).

These results from the articles and reviews that were collected have indicated that there is high chance for people over the age of 50 or more to acquire AMD and also is one of the main common concerns of blindness in the elderly. This review also deals in spreading awareness among people on the signs and symptoms and the various risk factors that people are prone to AMD. Also sufficient awareness on the disease its prevention and the various treatment available to treat patients with AMD. This review focuses on to reduce the frequency of AMD among people by spreading awareness on the same.

ABBREVIATIONS

- **AMD/ARMD** – Age Related Macular Degeneration
- **BM** - Bruch's membrane
- **RPE** - retinal pigment epithelium
- **MESA** - Multi-ethnic Study of Atherosclerosis
- **OCT**- Optical coherence tomography
- **AREDS1**-Age-Related Eye Disease Studies 1
- **AREDS2**- Age-Related Eye Disease Studies 2
- **VEGF**- vascular endothelial growth factor

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