

## Age Related Macular Degeneration in Coastal Communities: Review Article

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### ABSTRACT

**Introduction:** Many parts of the Indonesian coastline are open areas while at the same time there's not many place to take shelter causing exposure to sun rays to become more frequent. This condition puts the people around the coasts at high risk of various eye diseases such as keratitis, cataract, and Age-related macular degeneration (AMD).

**Content:** AMD is a chronic eye disease that causes central vision impairment due to degeneration of the retina in the macula. 8 million of people are enduring blindness due to retina complications not excluding AMD. Blue light and ultraviolet light that is contained within sun rays are the main cause of harm to tissues in the retina and reduce vision function.

**Conclusion:** The disease is irreversible but therapy can slow the progression of the disease, including laser therapy and anti-VEGF. Preventive action is the best management that can be done for coastal communities. The best action that can be done currently is preventing it by holding counseling sessions and increasing public awareness through education.

**Keywords:** Macular degeneration; coastal area; ultraviolet



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## Introduction

AMD is a chronic multifactorial eye disease that occurs due to disruption of the homeostatic mechanism or retinal cell apoptosis caused by chronic inflammation and oxidative stress resulting in the accumulation of lipid deposits, lipoproteins, and damage to the extracellular matrix<sup>1</sup>. Risk factors that cause AMD are genetic, diet, environmental factors such as sun exposure, lifestyle factors such as smoking and drinking alcohol, as well as medical factors such as cataracts and hypertension.<sup>1</sup>

AMD is the leading cause of blindness and visual impairment in the elderly population in Asian countries and worldwide. AMD is the third leading cause of blindness after cataracts and glaucoma with a contribution of about 8.7% of blindness in the world. The prevalence shows that around 196 million people in the world will experience visual impairment of AMD in 2020 with the incidence of AMD ranging from 1.4 to 3.5 per 1000 population.<sup>1,2</sup> There is currently no reliable data about the prevalence or incidence in Indonesia but it is predicted that the prevalence will double by 2050.<sup>3,4</sup>

Indonesia is an archipelagic country that has many coastal areas located on the equator, which is an area with consistent sun exposure throughout the year. The geographical location affects the exposure of sun radiation that enters the earth's surface. The more perpendicular the sun's rays, the more ultraviolet radiation (UVR) that reaches the earth's surface and the more cloudy or shady, the UVR will be smaller.<sup>3</sup>

## Definition

Retina has several structures such as Bruch's membrane, retinal pigment epithelium (RPE), and photoreceptor. Bruch's membrane is an extracellular matrix located between the RPE and the choroid, and plays a vital role as structural and functional support to the RPE. RPE performs specialized metabolic functions including processing lipids from photoreceptor turnover, synthesizing and absorbing lipids from the circulatory system. These structures are very vulnerable to light radiation especially in the macula which is the focus of light refraction. Macula is an area in the center of the retina, which harbors the area of sharpest vision.<sup>5</sup>

The coastal area is a transitional area between dry land ecosystems. Coast is an area several tens to hundreds of meters from land affected by sea tides (shores) to wet marine ecosystems. Coastal areas are open areas that often get sunlight and few shaded areas, causing coastal communities to be at risk for AMD because of UVR.<sup>3,6</sup> The International Commission on Non-Ionizing Radiation Protection (ICNIRP) defines several subgroups of ultraviolet or invisible radiation classified into UVA (315-400 nm), UVB (280-315 nm) and UVC (100-280 nm). The higher the wavelength, the more dangerous because it contains higher energy that can damage DNA or create free radicals.<sup>5,7,8</sup>

## **Epidemiology**

The prevalence of AMD in 2020 according to Wong et al is projected that 8 million people from 196 million population will experience blindness due to retinal complications including AMD.<sup>2,9,10</sup> Based on studies in the population aged 45-85 years, the average prevalence of AMD worldwide is around 8.7%, starting with the highest being 12.3% in Europe, 10.4% in North America, 7.5% in Asia and 7.5% in Africa.<sup>1</sup> The incidence of early-stage AMD is around 3.5 per 1000 population. Late-stage AMD is 1.4 per 1000 population. Dry type AMD and wet type AMD is 1.9 and 1.8 per 1000 population, respectively.<sup>1,2,11</sup>

## **Risk Factor**

There are several risk factors for AMD in the coastal areas including lifestyle and internal risk factors. Risk factors that correlate with personal habits or lifestyles are smoking, diet, and profession. Smoking increases the risk of developing AMD two to four times higher by affecting blood circulation health. The effects of smoking are, such as: lowering the amount of high-density lipoprotein, increasing fibrinogen, platelet aggregation, oxidative stress, and lipid peroxide, causing reduced plasma antioxidants and increasing levels of inflammations and cytokines.<sup>1,9</sup> Dietary consumption of lutein and zeaxanthin such as spinach, collard greens, kale, and consumption of fish oil or docosahexaenoic acid and eicosapentaenoic acid can reduce the risk of late stage AMD, but high sodium levels in marine fish and or due to high use of sodium salt in food processing in coastal communities, can increase the risk of hypertension and reduce the nutrients contained in these marine fish.<sup>1,8</sup> In addition, fisherman professional in the coastal area who fish during the day also increase the risk of AMD due to exposure to UVR through the reflection of the water or direct exposure.<sup>5,12</sup>

Internal risk factors include hypertension, age, and genetics. Hypertension can increase the risk of AMD because of its effect on blood vessels in the choroid. This increases the risk of vascular rupture leading to ischemia and retinal cell apoptosis in the macula.<sup>1,9</sup> Genetics contributes about 71% to increase the risk of developing AMD, which is higher than genetic influences on coronary heart disease.<sup>1,8,9</sup> Age is a risk factor that is strongly associated with the incidence of AMD. Studies show an increase in AMD cases from 3.5% at the age of 55-59 years to 17.6% at the age above 85 years.<sup>1,13</sup> Old age is a major risk factor for AMD because it is associated with structural and functional changes in the retina.<sup>1,14</sup>

## **Pathophysiology**

The eye has a protective mechanism against UVR but under certain conditions and prolonged exposure, UVR still can reach and cause retinal damage. Ultraviolet C (UVC) is mostly absorbed by nucleotide bases and aromatic amino acids so that little passes through the cornea and lens but higher wavelengths, UVA and UVB, can reach and damage the retina. High doses of UVR cause photokeratitis and photo

conjunctivitis, low doses of chronic UVR can cause cataracts, pterygium, squamous cell carcinoma of the cornea and conjunctiva, and AMD.<sup>1,5</sup>

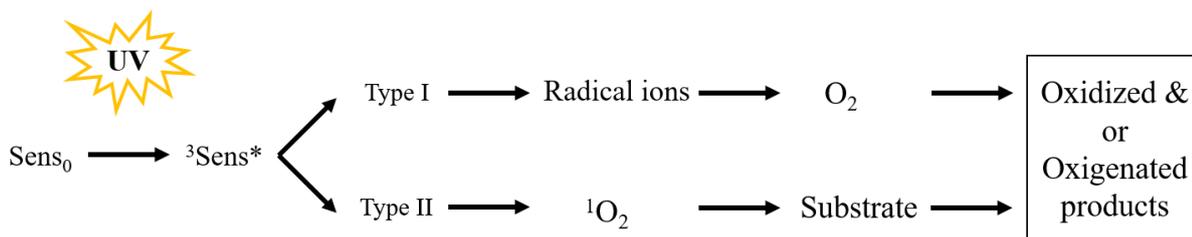


Figure 1. Diagram of ROS generation due to UVR exposure, type 1 and type 2 reaction.<sup>5</sup>

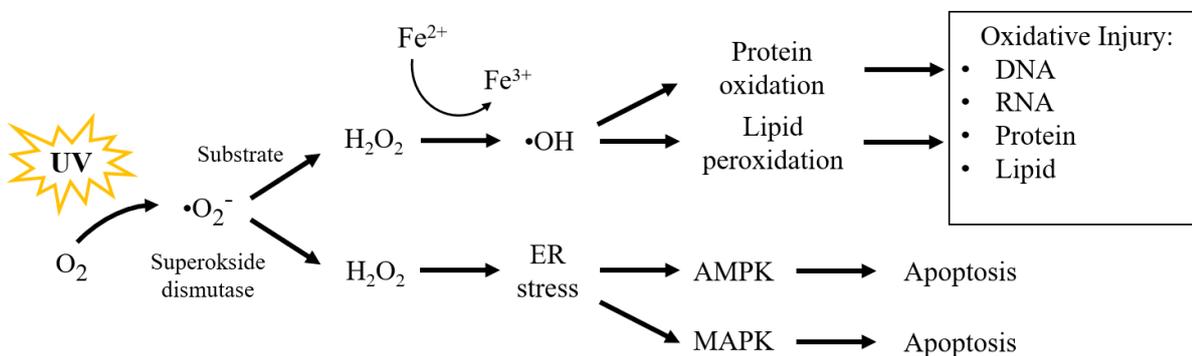


Figure 2. Diagram of ROS generation due to UVR exposure, delayed reaction.<sup>5</sup>

UVR can cause photochemical damage resulting in the formation of oxidation molecule in retina especially macula.<sup>5,10</sup> Retina is probably the tissue that contain the highest endogenous photosensitizers or chromophore that can be excited by light as a consequence, it is highly sensitive to oxidative damage. Chromophore molecules in the retina that can be oxidized are photoreceptor pigments, proteins, flavoproteins, and pigment granules melanin and lipofuscin. There are 3 different ways UVR excites chromophores and produces free radicals, type 1, 2, and delayed reactions. In type 1, after the chromophores are excited by UVR into a triplet state, it undergoes a direct electron or hydrogen exchange with the substrate, creating a free-radical intermediate. Then, this free-radical intermediate reacts with additional substrate or oxygen, which is available a lot in the retina, to create peroxidation products. In type 2, triplet chromophore directly reacts with oxygen without free-radical intermediate and produces singlet oxygen. In the end, these two type ways can produce reactive free radicals if they meet substrates like lipids in RPE and create peroxidation reaction products that damage nearby retina tissue. In the delayed type, UVR oxidizes oxygen into a superoxide radical. Then, it reacts with an additional substrate or superoxide

dismutase that generates the electric neutral hydrogen peroxide ( $H_2O_2$ ). In the presence of some metal ions  $H_2O_2$ , a non-radical oxygen species forms the highly reactive and most powerful free radical ( $\bullet OH$ ). It's called delayed because it triggers delayed oxidative responses that may persist after irradiation is stopped. UVA can cause type 1 and type 2 reactions because it has higher energy to initiate oxidation through the photosensitization mechanism. Meanwhile, UVB can only generate delayed type reaction.<sup>5</sup>

Free radicals  $\bullet OH$  reacts with other molecules such as lipids to form lipid peroxidation which damages the structure of cell membranes or reacts with protein molecules to form protein oxidase which can damage the sensorineural and retinal structure. Lifelong chronic exposure to UVR causes a build-up of oxidative damage that weakens the protective layer of the eye thereby contributing to macular degeneration.<sup>5</sup> In addition, accumulation of  $H_2O_2$  also accelerates and stimulates the formation of ceramide-dependent cell apoptosis which induces endoplasmic reticulum stress that will initiate the activation of the AMP-activated protein kinase (AMPK) and mitogen-activated protein kinase that end in cell apoptosis cascades.<sup>15</sup>

## Clinical Manifestations

Clinical Manifestations felt by patients include:

1. Difficulty seeing in low-contrast, dim, or dark-adapted conditions.<sup>1,16</sup>
2. Loss of ability to read and recognize faces.<sup>1</sup>
3. Decreased visual acuity (blurry) especially in the central visual field.<sup>1,16</sup>
4. Visual distortion (straight lines become wavy or distorted), objects appear larger or smaller.<sup>1,9,16</sup>

A physical examinations that can be tested include:

1. Decreased central visual field.<sup>1</sup>
2. Amsler grid test, the patient sees dots and straight lines become wavy or distorted.<sup>9</sup>
3. Funduscopy, early-stage AMD found fatty deposits (drusen) on the macula, late stage may reveal geographic macular atrophy in dry type AMD or wet type AMD it may be neovascular; fibrovascular, serous or hemorrhage retinal detachment, subretinal epithelial hemorrhage or fibrous tissue.<sup>1</sup>

## Treatment and Management

AMD is an irreversible degenerative disease and available therapies only prevent the progression of wet-type AMD such as photodynamic laser therapy, photocoagulation, and anti-VEGF.<sup>1,5,9</sup> Therefore, counseling and education are the best way to manage AMD in coastal areas. By providing education and counseling, people can understand more about AMD so they can change lifestyle habits and take preventive measures. In addition, more specifically AMD prevention can be done by:

1. Conduct counseling related to risk factors, prognosis and complications, and the importance of maintaining eye health and routine eye health checks.<sup>1</sup>
2. Wearing sunglasses during the day.<sup>12</sup>
3. Routine physical activity and smoking cessation.<sup>1,9,17</sup>
4. Consumption of vegetables such as spinach, and collard greens which are high in lutein and zeaxanthin as antioxidants reduce free radicals caused by UVR and *polyunsaturated fat* reduces fat deposits in the macula.<sup>1,9,18</sup>
5. Consumption of vitamin C, vitamin E, beta carotene, and zinc can prevent and reduce 25% progression in the next 5 years.<sup>1</sup>

## Conclusion

Indonesia is an archipelagic country with many coastal areas exposed to UVR throughout the year due to its geographical location. AMD is a multifactorial degenerative disease that one of the risk factors is sun exposure. This disease is characterized by a decrease in central vision without affecting peripheral vision. This disease cannot be cured but therapy can slow the progression of the disease, including laser therapy and anti-VEGF. Preventive action is the best management that can be done for coastal communities.

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