# Evaluation of Risk Factors Affiliated with Age Related Macular Degeneration

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### **Keywords**

Age Related, Macular Degeneration, Risk factors, Optical Coherence Tomography

## Abstract

Objective - The research aimed to evaluate the risk factors affiliated with ARMD.

Materials & Method - The research used a cross sectional design, elderly patients of 50 years age group. All the eligible patients were assessed on the basis occupation, h/o smoking, diabetes, hypertension, obesity & pigment abnormalities by performing External examination with torchlight, Snellen's chart for visual acuity, Slit lamp bio-microscopy, Amsler grid, Fundus Examination with Direct ophthalmoscope, 90 D and indirect-ophthalmoscope after full dilatation, Optical coherence tomography.

Results - In this research it was observed that ARMD was much higher in housewives (34 %) and shopkeepers (12%) were most affected. History of smoking (42%) was calculated to be less associated with the patients of ARMD. Majority patients presented with intermediate drusens on fundus finding followed by large (20%), geographical atrophy (18%), CNVM (11%) and few small drusens (11%). Dry (NON-EXUDATIVE) ARMD (89%) was seen higher than WET(EXUDATIVE) ARMD (11%). The amount of obesity and ARMD had very less significance (40%). History of diabetes (75%) and hypertension (69%) were found to have strong association.

Conclusion - The results revealed that history of smoking had higher odds to exhibit ARMD, in comparison to diabetes, hypertension and obesity.

### 1. Introduction

One of the main causes of blindness in the elderly globally is age-related macular degeneration. The core region of the retina known as the macula is impacted by this bilateral ocular disease. According to WHO estimates, "20 to 25 million people with AMD", of which 8 million have significant visual impairment. If it goes undiagnosed, untreated, or uncontrolled, the WHO projects that the number will increase to "288 million by 2040". The developing world, notably India, is being badly impacted by this terrifying disease, which accounts for "8.7% of all blindness worldwide" <sup>[1-5]</sup>.

The majority of useful photopic vision is produced by the macula, which makes up only 4% of the retinal surface. Even though it just has a 6 mm diameter, it takes up about 10% of the whole visual field. The patient complains of blurry vision and a

loss of contrast sensitivity. Although angiogenesis therapy, which is costly and less widely available but has been recognised as an effective treatment option, has significantly improved the management of wet ARMD, dry ARMD still needs to be addressed [6,7]. More than 90% of patients with AMD in both industrialised and developing countries have non-exudative (dry) age-related macular degeneration. Loss of central vision is commonly noticed as a late symptom of dry AMD as it proceeds to retinal atrophy and central retinal degeneration. Generally speaking, nonexudative AMD progresses far more slowly (over decades) than exudative (wet) AMD, which takes place within months.

The exudative form of advanced AMD, which accounts for the majority of the estimated 1.75 million cases in the developed world, progresses in about 10-20% of individuals with nonexudative AMD over time.

People with European (white) heritage had higher rates of early and late-stage illness than people with African ancestry in the Baltimore Eye Study <sup>[8]</sup>. The "Beaver Dam Eye Investigation", the first "sizable population-based study" to look at the long-term relationships between "smoking and the incidence of AMD", found a favourable relationship between "smoking and early AMD incidence but not late AMD incidence" [9]. AMD has demonstrated a substantial relationship with other systemic illness risk factors, such as cardiovascular disease, in addition to smoking <sup>[10,11]</sup>, elevated cholesterol level <sup>[12]</sup> and hypertension <sup>[13]</sup>.

"AREDS" stand for "Age Related Eye Disease Study" which was conducted under NIH as a clinical trial over more than 5,000 with AMD & ended in 2001. It was inferred with a specific formula of antioxidants and zinc supplementation; the progression of intermediate AMD could be slowed down.

Following which AREDS 2 was conducted in 2013 in which beta carotene was substituted with lutein and zeaxanthin, since beta carotene was seen as a strong element in view of increase risk of lung cancer in smokers. The results showed decrease of AMD by 19% and of vision loss by 25%.

#### 2. Materials and Method

The present cross-sectional study was conducted in the OPD of ophthalmology at Santosh Medical College and Hospital, Ghaziabad to evaluate the risk factors affiliated with ARMD in above 50 years.

"We have selected 100 cases of above 50 years age group & the information regarding age, gender, race, details of ocular examination, investigations, diagnosis and systemic disease association, if any were recorded for all patients".

#### Inclusion Criteria:

All adults of age 50 years and above, presenting in Ophthalmology OPD in Santosh medical college & hospital Ghaziabad.

#### Exclusion Criteria:

1.Adults less than 50 years of age

2.Adults suffering from any other systemic disease other than Diabetes and Hypertension

3. Patients having other Retinal Pathologies

Data Collection Tools and Techniques: -

"The diagnosis for ARMD is based on a detailed clinical history, torchlight examination, ophthalmological examination & general physical examination and specific test"

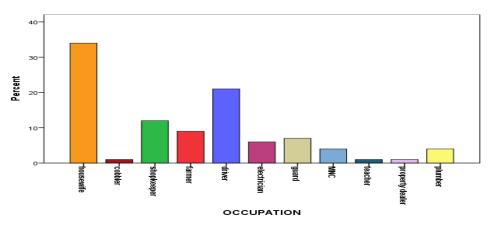
Ocular Examination Included:-

- · External examination with torchlight
- Snellens chart for visual acuity
- Slit lamp bio-microscopy
- Amsler grid
- Fundus Examination with Direct ophthalmoscope, 90D and indirect ophthalmoscope after full dilatation.
- Optical coherence tomography.

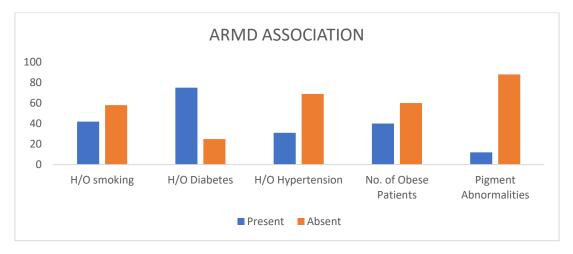


### 3. Result

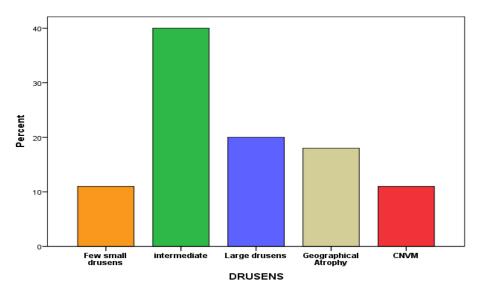
Occupation of Subjects Enrolled in the Study is Depicted in Figure 1.



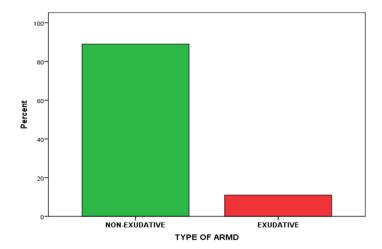
Other Risk Factors Associated with ARMD Depicted in Figure 2.



Grade of ARMD along with the Type of Drusen are Depicted in Figure 3.



Type of ARMD is Depicted in **Figure 4**.



"On binomial logistic regression to ascertain the effects of age, gender, history of smoking, obesity and hyperglycemia on the likelihood that participants having ARMD, the logistic regression model was statistically significant,  $\chi^2(5) = 40.145$ , p & lt; .001. The model explained 66.1% (Nagelkerke R2) of the variance in ARMD and correctly classified 97.0% of cases. Sensitivity was 81.8%,

specificity was 98.9%, positive predictive value was 90% and negative predictive value was 97.7%. Of the five predictor variables only three were statistically significant: age, gender and history of smoking (as shown in Table 1). Females had 2.4 times higher odds to exhibit ARMD than males (OR=2.4). Old age (OR=1.20) was associated with an increased likelihood of exhibiting ARMD".

Table	1.	Logistic	Regression	

Independent variables	В	S.E.	Wald			Exp(B)	95% C.I.for EXP(B)	
				df	Sig.		Lower	Upper
age	.187	.089	4.423	1	.035	2.41	2.206	2.868
SEX	.865	1.399	.383	1	.053	2.375	.153	36.853
OBESITY	-20.046	6559.448	.000	1	.998	.000	.000	•
HISTORY OF SMOKING	-1.891	.950	3.962	1	.047	.302	.046	1.942
DIAB	.519	9551.513	.000	1	1.000	1.681	.000	•
Constant	8.033	6559.452	.000	1	.094	3080.598		

a. Variable(s) entered on step 1: Age, SEX, OBESITY, HISTORY OF SMOKING, DIABETES.

#### 4. Discussion

As avoidable blindness due to cataract decreases, age-related causes of blindness have now assumed

greater significance <sup>[14]</sup>. Epidemiological studies have found a number of risk factors associated with the development of macular degeneration including advancing age, genetics, ethnicity, smoking,

sunlight exposure, diet, hypertension, iris colour and body mass index <sup>[15,16]</sup>. The present cross-sectional study evaluated risk factors for development of ARMD in the study cohort <sup>[16]</sup>. There exists considerable evidence to suggest higher risk of ARMD in women compared with men (OR, 1.2; 95% CI, 1.0-1.5). In the present study, females had 2.4 times higher odds to exhibit ARMD than males (OR=2.4).

A study conducted in Nepal by Pokhrel et al and another study by Hazin et al also found a higher risk ARMD in women [17]. However, studies conducted in America and Japan have found increased risk of ARMD in men. On the contrary, Kandy eye study (Sri Lanka) did not find any difference in the risk of ARMD between men and women [18]. One might argue that females have a longer life span and consequently, a higher incidence of ARMD. Having said this, pipe smoking among males may make them more vulnerable to macular degeneration. Patients with history of smoking exhibited higher odds of having ARMD in a logistic regression model in the present study. The "Beaver Dam Eye Study" found that men who smoked more cigarettes were more likely to develop early AMD [19]. At 10 year follow up, concrete evidence was found that smoking causes progression of ARMD. The "Blue Mountains Eye Study" was conducted in Australia <sup>[20]</sup>. "It recruited 3654 patients and found that smokers had a 4 fold increase in the risk of late AMD compared with non smokers (RR = 3.9; 95% CI: 1.7 to 8.8) at 10 years follow up. A pooled analysis of the 5 year results from these studies found a 3 fold association of smoking with the development of AMD [20,21]. The Physicians & Health Study and the Nurses' Health Study also found evidence that smokers of 20 or more cigarettes per day had a 2 fold increased risk compared with non smokers on 7 year follow up" [22,23].

The "Age-Related Eye Disease Research (AREDS)" examined the progression of AMD and cataract in 4757 people enrolled between 1992 and 1998 in a multicenter, longitudinal study. According to this investigation, smoking was linked to all three of the AMD groups with the greatest severity [24]. Chronic inhalation of cigarette smoke may result in oxidative stress, vascular alterations, and inflammation, all of which raise the risk of AMD. Second, it alters RPE cells at the cellular level. Additionally, thrombosis,

endothelial vascular inflammation, and dysregulation have all been linked to smoking's role in the development of atherosclerosis. Studies have found conflicting evidence on the association of hypertension and ARMD. Hypertension was associated with ARMD in the United Kingdom; stage 2 hypertension (OR, 3.21; 95% CI, 1.14-8.98), was positively associated with neovascular AMD. In our study also, we could not find a significant association of hypertension with ARMD. The shortcomings of the present study were that sample size was small which may not be representative of the entire population. Second, slit lamp biomicroscopic screening of subjects may have underestimated detection of early ARMD changes adding to bias in the study. Screening subjects with digital retinal scans in a relatively large sample size of patients could provide deeper insights into prevalence rates and identification of risk factors.

#### 5. Conclusion

According to our study the age distribution was appreciated more in between 50-60 following this was between 60-70. The gender distribution was seen much higher in males than in females. The highest amount of people affected were housewives and shopkeepers. History of smoking was calculated to be less associated with the patients of ARMD. Although history of smoking was affected with Non-Exudative ARMD. Majority patients presented with intermediate drusens on fundus finding followed by large, geographical atrophy, CNVM and few small drusens. Dry (NON-EXUDATIVE) ARMD was seen higher than WET(EXUDATIVE) ARMD. The amount of obesity and ARMD had very less significance in our study. History of diabetes and hypertension were found to have strong association.

In conclusion, the results of the present crosssectional study revealed that the logistic regression model revealed that age, female gender and history of smoking had higher odds to exhibit ARMD, in comparison to diabetes, hypertension and obesity.

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**Conflict of Interest:** The authors declare that they have no competing interests.

### Informed consent taken

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### References

- [1] Klein R, Klein BE, Cruickshanks KJ. The Prevalence of age-related maculopathy by geographic region and ethnicity. Prog Retin Eye Res; 1999; 18: 371–89.
- [2] Mitchell P, Smith W, Attebo K, Wang JJ. Prevalence of age-related maculopathy in Australia. The Blue Mountains Eye Study Ophthalmology; 1995; 102: 1450–60.
- [3] Klaver CC, Assink JJ, van Leeuwen R, et al. Incidence and progression rates of agerelated maculopathy: the Rotterdam Study. Invest Ophthalmol Vis Sci; 2001; 42: 2237–41.
- [4] Kawasaki R, Yasuda M, Song SJ, et al. The prevalence of age-related macular degeneration in Asians: a systematic review and meta-analysis. Ophthalmology; 2010; 117: 921–27.
- [5] Wong TY, Chakravarthy U, Klein R, et al. The natural history and prognosis of neovascular age-related macular degeneration: a systematic review of the literature and meta-analysis. Ophthalmology; 2008; 115: 116–26.
- [6] Bressler NM. Age-related macular degeneration is the leading cause of blindness. JAMA; 2004; 291: 1900–01.
- [7] Bressler NM, Doan QV, Varma R, et al. Estimated cases of legal blindness and avoided visual impairment using ranibizumab for choroidal neovascularization: non-Hispanic white population in the United States with agerelated macular degeneration. Arch Ophthalmol; 2011; 129: 709-17.
- [8] Klein R, Klein BE, Knudtson MD, et al. Prevalence of age-related macular degeneration in 4 racial/ethnic groups in the multi-ethnic study of atherosclerosis. Ophthalmology; 2006; 113: 373–80.
- [9] Klein RKlein BETomany SCMoss SE Ten-year incidence of age-related maculopathy and smoking and drinking:

the Beaver Dam Eye Study. Am J Epidemiol; 2002; 156 (7)

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- [10] Snow KKSeddon JM Do age-related macular degeneration and cardiovascular disease share common antecedents? Ophthalmic Epidemiol; 1999; 6 (2)
- [11] Tomany SCWang JJvan Leeuwen R et al. Risk factors for incident age-related macular degeneration: pooled findings from 3 continents. Ophthalmology; 2004; 111 (7)
- [12] Hyman, LSchachat, APHe, QLeske MC. Age-Related Macular Degeneration Risk Factors Study Group, Hypertension, cardiovascular disease, and age-related macular degeneration. Arch Ophthalmol; 2000; 118 (3)
- [13] Klein, RKlein, BEKTomany,
  SCCruickshanks KJ. The association of cardiovascular disease with the long-term incidence of age-related maculopathy: the Beaver Dam Eye Study. Ophthalmology; 2003; 110 (6)
- [14] Fine SL, Berger JW, Maguire MG, Ho AC. Age-related macular degeneration. N EnglJ Med; 2000; 342 (7): 483-92.
- [15] Hageman GS, Luthert PJ, Victor Chong NH, Johnson LV, Anderson DH, Mullins RF. An integrated hypothesis that considers drusen as biomarkers of immune-mediated processes at the RPE-Bruch's membrane interface in aging and age-related macular, Department of Ophthalmology and Visual Sciences, The University of Iowa Center for Macular Degeneration, USA.
- [16] Sucheta R Kulkarni, Supriya R Aghashe, Rajiv B Khandekar, Madan D Deshpande. Prevalence and determinants of age-related macular degeneration in the 50 years and older population: A hospital based study in Maharashtra, India: Indian J Ophthalmol; 2013 May; 61 (5): 196–201.
- [17] Pokharel S, Malla OK, Pradhananga CL, Joshi SN. A Pattern of Age-related Macular Degeneration: Department of Ophthalmology, Kathmandu Medical College, Department of Ophthalmology, Institute of Medicine, Maharaj- gunj, Kathmandu, Nepal J Nepal Med Assoc; 2009; 48 (175): 217-20.

- [18] L A Goold, K Edussuriya, S Sennanayake, T Senaratne D Selva, T R Sullivan, R J Casson, BMJ. Prevalence and determinants of age-related macular degeneration in central Sri Lanka: the Kandy Eye Study; 2010.
- [19] R. Klein, B.E. K. Klein, M.D. Knudtson, S.M. Meuer, S.M. Meuer R. The Fifteen– Year Incidence of Age–Related Macular Degeneration: The Beaver Dam Eye Study, Investigative Ophthalmology & Visual Science, Vol.47. Gangnon: May 2006. 1129.
- [20] Paul Mitchell, MD, PhD; Jie Jin Wang, MMed, PhD; Wayne Smith, MBBS, PhD; et al Stephen R. Leeder MBBS, PhD. Smoking and the 5-Year Incidence of Age-Related Maculopathy: The Blue Mountains Eye Study, Arch Ophthalmol; 2002.
- [21] Praveen K, Nirmalan, MD, MPH; Joanne Katz, PhD; Alan L. Robin, MD; et al James M. Tielsch, PhD; Perumalsamy Namperumalsamy, MD; Ramasamy Kim, MD; V. Narendran, MD; Rengappa Ramakrishnan, MD; Ramasamy Krishnadas, MD; Ravilla D. Thulasiraj, MBA; Eric Suan, MD. Prevalence of

Vitreoretinal Disorders in a Rural Population of Southern India: The Aravind Comprehensive Eye Study, Arch Ophthalmol; 2004;122 (4): 581-586.

- [22] Sannapaneni Krishnaiah, Taraprasad Das, Praveen K. Nirmalan, ishita Nutheti, Bindiganavale R. Shamanna, Gullapalli N. Rao, Ravi Thomas. Risk Factors for Age-Related Macular Degeneration: Findings from the Andhra Pradesh Eye Disease Study, Investigative Ophthalmology & Visual Science, Vol.46. South India: December 2005, 4442-4449.
- [23] Augood CF letcher, A Bentham G et al. Methods for a population-based study of the prevalence of age-related maculopathy and macular degeneration in elderly European populations: the EUREYE study: Ophthalmic Epidemiol; 2006.
- [24] AREDS2 Research Group. "Lutein/Zeaxanthin and Omega-3 Fatty Acids for Age-Related Macular Degeneration. The Age-Related Eye Disease Study 2 (AREDS2) Controlled Randomized Clinical Trial." JAMA, published online May.