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PREVALENCE AND ASSOCIATED RISK FACTORS OF AGE RELATED MACULAR DEGENERATION IN PATIENTS ABOVE 50 YEARS - A CROSS SECTIONAL STUDY.

Ophthalmology

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ABSTRACT

Purpose- To determine prevalence of AMD in patients of ≥50 years of age and to study risk factors of AMD.
Methods- This is a cross-sectional hospital based study. Patients attending hospital OPD during August 2011 to January 2013 who were ≥ 50 years of age were included. Patients were interviewed in detail to collect the information on risk factors (E.g. age, sex, family history of AMD, smoking, alcohol, hypertension, diabetes, cardiovascular disease, prior cataract surgery, BMI). All patients underwent fundus photography and all photographs were classified according to AREDS grading system of AMD. Total of 6954 patients were enrolled. Statistical software STATA version 10.0 was used for statistical analysis.
Results- AMD was found in 153 patients, prevalence of AMD was 2.2% (95% CI, 1.86%-2.57%). Out of 10 risk factors studied 5 were found statistically significant on bivariate analysis i.e. age, smoking, prior cataract surgery, alcohol and cardiovascular disease. These risk factors were also found significant in multivariate analysis. Prevalence of AMD was significantly higher in smokers (Chi2=33.89, P value=<0.0001) and alcoholics (Chi2=20.92, p value =<0.0001).
Conclusion- Three strong and consistent risk factors (Age, smoking, prior cataract surgery) & two significant and moderate risk factors (alcohol, cardiovascular disease) were identified.

KEYWORDS

Prevalence, Macular degeneration, smoking, alcoholic

INTRODUCTION

Age-related macular degeneration (AMD) is a common, chronic, progressive degenerative disorder of the macula which affects older individuals and causes central visual loss as a result of drusen deposition, geographical atrophy, serous detachment of the retinal pigment epithelium and neovascularization.

Age-related macular degeneration (AMD) is the leading cause of irreversible vision loss among the elderly and is a major risk factor for disability in the older population. It substantially affects the quality of life of an individual as documented by clinical depression in almost one third of those who have this condition.[1] Among individuals who have vision loss from AMD, 60% report significant declines in their ability to participate in valued activities.[2]

Age-related macular degeneration (AMD) is the leading cause of blindness among people aged 50 years and older worldwide affecting 30–50 million individuals.[3,4,5] The age related macular degeneration is the third most common cause of blindness worldwide. Krishnaiah et al [6] (2005) found that the age-gender-area–adjusted prevalence of AMD in Indian population was 1.82%.

With rapidly increasing aging population in India (life expectancy of: 69.9 years) and with blindness due to cataract being addressed more vigorously, the age-related blinding causes of posterior segment will be more important in the coming years.7 The demography of India is remarkably diverse. Epidemiological findings of aging population in Western India could differ from other parts. Our study in Nagpur, therefore, will add to the knowledge of epidemiology of AMD in Central India and also enable the health planners to determine risk factors and propose preventive measures.

Progressive degeneration of the choriocapillaris, retinal pigment epithelium (RPE), and photoreceptors causes Loss of visual acuity, although the earliest manifestation of the disease appears to be abnormalities within Bruch's membrane.

Advanced AMD are often classified broadly into two types: dry and wet. Majority of all diagnosed cases accounts for dry AMD, wet AMD is responsible for the majority of the severe vision loss and it generally occurs over weeks to months. Commonest cause of neovascularization is severe vision loss, geographic atrophy (GA), the foremost advanced form of dry AMD, can also cause significant loss of vision.

The study of risk factors for AMD is important in understanding the disease and suggests preventive measures that can retard or control disease progression. Several studies have reported modifiable and non-modifiable risk factors for AMD.[3,8-22] Although several factors were identified, only age, smoking, hypertension, and obesity have been confirmed as increasing the risk of AMD.[23,24] Cataract surgery is also a significant predictor, with a four- and threefold increase in the risk of neovascular AMD and geographic atrophy, respectively.[23,24]

Krishnaiah et al [6] (2005) concluded that smoking is the most consistent risk factor associated with the prevalence of AMD. Shih-Jen Chen et al [25] (2008) in his Shihpai Eye Study found that heavy alcohol drinking is positively associated with early AMD.

With the introduction of new and effective treatments for AMD, there's a robust rationale for early identification of persons at highest risk of progression to the late stages, as timely treatment given at the onset of AMD will lead to better visual outcomes.

In this regard, various risk factors for AMD have been identified, including genetic (e.g., complement factor H polymorphisms), demographic (e.g., ethnicity), nutritional (e.g., antioxidant vitamins, dietary fats or fish), lifestyle (e.g., smoking), medical (e.g., cardiovascular risk factors), environmental (e.g., sun exposure), and ocular factors.[26] However, the evidence and strength of association remain variable in the literature. Furthermore, a number of these risk factors (e.g., diet and genetic factors) aren't easily measured in routine clinical practice.

Therefore, it was our view that more precise estimates of risk factors that could be assessed through routine history taking would be of value for appropriate counseling and referral. This study was conducted to determine the magnitude of AMD among the native population aged 50 years and older in Nagpur city who visited the ophthalmology department of our institute & to determine the association of potential risk factors in AMD.

Methodology

This is a cross-sectional hospital based study conducted from August 2011 to January 2013 in Mahatme Eye bank & Eye Hospital, Nagpur, Maharashtra, India, to determine prevalence of AMD in patients of ≥50 years of age and to study risk factors of AMD. The study was approved by the institutional ethics committee. 6954 patients attending hospital

outpatient department who were ≥ 50 years of age were included after taking informed consent.

Inclusion criteria:

- Age ≥ 50 years of either sex
- Diagnostic criteria of age related macular degeneration were as follows: [47]

AMD was considered to be present when one of the following was present in macular area-

1. Large drusens (yellow deposits under retinal pigment epithelium)
2. Hyperpigmentation or Hypopigmentation of retinal pigment epithelium
3. Atrophic macular degeneration known as geographic atrophy (areas of atrophy of retinal pigment epithelium & choriocapillaries)
4. Neovascular macular degeneration (Serous retinal pigment epithelial detachment & Macular neovascularization)

Exclusion criteria were patients having other retinal diseases E.g. diabetic retinal diseases, having bilateral media opacities preventing evaluation of macula E.g. bilateral mature cataract, patients in whom dilatation of pupil was contraindicated E.g. angle closure glaucoma, familial dominant drusens, Type 2 membranoproliferative glomerulonephritis (drusen like lesions) and causes of retinal flecks such as Stargardt disease & fundus flavimaculatus, Benign flecked retina and Alport syndrome.

A pretested standardized questionnaire was used to collect demographic data, information on risk factors of systemic diseases, personal habits and family history was evaluated. After collecting demographic data, specific history for following ten potential risk factors of AMD was obtained from responders, i.e. Age, Sex, Family history of AMD, History of smoking, alcohol consumption, Hypertension, Diabetes, Prior cataract surgery, cardiovascular disease and body mass index. Systemic examination included height, weight & blood pressure measurement.

All the patients underwent detail examination regarding UCVA, BCVA, Anterior segment and fundus examination.

Stereo examination of the disc and macula was performed with a 90-D lens for slit-lamp biomicroscopy; 20-D lens was used for indirect ophthalmoscopy. Posterior segment was evaluated with a fundus camera. All photographs were classified according to Age-Related Eye Disease Study (AREDS) classification and grading system of age-related macular degeneration.[28]

Hard drusens were defined as small, round, flat, yellow-white deposits, and soft drusens as large, round yellow-white deposits. The retinal pigment epithelial changes appeared as areas of hyper- or hypopigmentation. Geographic atrophy was defined as a large area of well-demarcated hypopigmented retinal pigment epithelium, often with apparent choroidal vessels. Choroidal neovascular membrane was defined as a green-gray lesion, with or without subretinal hemorrhage or exudate.[29]

Any other abnormality detected was also documented. The cases of AMD thus detected were also confirmed by the senior consultants. Whereas age-related macular degeneration was classified as wet (neovascular) or dry (atrophic) and they were combined for analysis. The patients who were diagnosed as AMD were subjected to further investigations, e.g. FFA, OCT & treated, if required.

Smoking Status- For this analysis, subjects were categorized as never smokers and smokers. Subjects who had never smoked, or had smoked for less than 1 year were considered to be "never smokers".

Cumulative Smoking Dose- For this analysis, smokers were categorized as light and heavy smoker, based on cigarette and cigar pack years. The pack-year was calculated by multiplying the number of packs of cigarettes or cigars smoked per day by the number of years the person has smoked. We used the 25th percentile pack years to categorize cigarette or cigar smokers as light and heavy smokers.[6]

Alcohol consumption- A person who drinks alcohol for 3 to 4 days a week or more was considered to be heavy drinker.[6]

Body mass index (BMI) was calculated from the measured height and weight according to the formula: weight (in kilograms) divided by height (in meters) squared. Categories used included underweight (BMI <20), normal (20-25), overweight (>25- <30), and obese (BMI ≥30).[30]

Continuous variable like age and body mass index was presented as mean ±SD & median was also calculated. Categorical variables (e.g. sex, family history, smoking, history of prior cataract surgery, hypertension, diabetes, alcohol consumption, history of cardiovascular disease) were expressed in actual numbers and percentage. To assess the association between age and prevalence of AMD, chi-square test for linear trend was used. Bivariate analysis was performed to find association between various risk factors and prevalence of AMD. Chi-square test and Fisher exact test for small numbers was used wherever applicable. Odds ratio and 95% confidence interval were calculated. Those variables which were significant on bivariate analysis, were included in multivariate regression analysis model. All the tests were two-tailed. $p<0.05$ was considered as statistically significant. Statistical software STATA version 10.0 was used for statistical analysis.

Result

Either form of AMD (dry or wet) was detected in 153 of 6954 participants. The prevalence of AMD was 2.2% (95% CI, 1.86%-2.57%). The highest number of patients were found in age group of 60-69 years (total patients=3111, AMD patients=65) but highest prevalence of AMD was found in ≥80 years of patients (6.48%). Chi-square for linear trend=59.33, p value =<0.0001.

AMD was present in 33 subjects of ≤60 years of age and 120 subjects of >60 years of age. The adjusted prevalence of AMD was significantly higher in those >60 years of age (OR=2.51, 95% CI [1.69-3.83], p=<0.0001). The median age of the subjects was 62 (61.85±7.89) years ranging from 50 to 89 years.

Prevalence of AMD in male & female groups was almost same (2.04% and 2.33% respectively). Odds Ratio=1.14, 95% CI [0.82-1.60], p value=0.4179 (not significant). The family history of AMD was present in only 1 patient among the patients of AMD. Odds Ratio=3.18, 95% CI [0.07-21.24], p value =0.2378 (not significant).

Prevalence of AMD was significantly higher in smokers (4.18%) Table 1.

Table 1: Smoking status of study subjects

Smoking status	Total Population N =6954	AMD n=153(%)	NO AMD
Smokers	932	39(4.18%)	893
Non-smokers	6022	114(1.89%)	5908
Odds Ratio=2.26, 95% CI [1.52-3.30], p value =<0.0001 (highly significant).			

Prevalence of AMD was significantly higher in heavy smokers (5.63%) as compared to light smokers (1.92%) and non-smokers (1.89%) (Chi-square=33.89, P value=<0.0001, highly significant). While in alcoholics, prevalence of AMD was (3.26%), Odds Ratio=1.68, 95% CI [1.14-2.43], p value=0.0041.

AMD was significantly higher in heavy drinkers (6.51%), Chi2=20.92, p=<0.0001 (highly significant). Prevalence of AMD was almost same in non-drinkers and light drinkers (1.95% and 2.60%) which was not significant (Chi-square=1.874, p value =0.171).

Prevalence of AMD in hypertensive, normotensive, diabetic and non-diabetic patients were 2.36%, 2.04%, 0.83% & 2.27%, which were not statistically significant (p≥0.05). While in patients with history of cardiovascular disease it was (3.9%), Odds Ratio=1.96, 95% CI [1.21-3.06], p value =0.0020.

Table 2: Prior cataract surgery in study subjects

Prior cataract surgery	Total Population N =6954	AMD n=153(%)	NO AMD
Present	516	46(8.91%)	470
Absent	6438	107(1.66%)	6331
Odds Ratio=5.79, 95% CI [3.95-8.36], p value =<0.0001 (highly significant).			

Prevalence of AMD in underweight and obese patients was comparatively higher (2.33% and 3.15% respectively) than in normal and overweight patients (2.08% and 1.54% respectively). Odds

Ratio=0.93, 95% CI [0.53-1.54], p value =0.786. Whereas in prior cataract surgery patients it was highly significant. (Table 2)

Table 3: Multivariable Logistic Regression Analyses for Associations between Potential Risk Factors and AMD (N =6954)

Variables	Adjusted odds ratio	95% CI	p value
Age	4.15	2.73-6.30	<0.0001
Smoking	2.28	1.56-3.34	<0.0001
Alcohol consumption	1.57	1.08-2.28	0.016
Cardiovascular disease	2.22	1.41-3.49	0.001
Prior cataract surgery	8.08	5.50-11.87	<0.0001

As shown in the above table 3, all the variables which were statistically significant in bivariate analysis were also statistically significant in Multivariable Logistic Regression Analyses with p value <0.0001.

Table 4: Number of significant risk factors in study subjects

Number of risk factors	Total Population N =6954	AMD n=153	NO AMD
Zero	1497	8(0.53%)	1489
Single	3691	57 (1.54%)	3634
Two	1494	56 (3.74%)	1438
Three	251	25 (9.96%)	226
Four	21	7 (33.33%)	14
Five	0	0	0
chi2 for linear trend=127.75, p value =<0.0001 (highly significant).			

As the number of significant risk factors increases, prevalence of AMD increases significantly. There was no patient with all five significant risk factors (Table 4).

DISCUSSION

Total 6954 patients underwent detailed eye examination including fundus photo, out of which 153 patients were diagnosed having AMD in at least one eye.

Prevalence of AMD in this population was 2.2% (95% CI, 1.86%-2.57%). Prevalence of AMD in- Andhra Pradesh Eye Disease Study [6] was 1.82% and in white population- 1.9% in Blue Mountain eye study[31] while 1.7% in Rotterdam eye study.[31]

Jyh Haur woo et al [32] in his study reported the prevalence of AMD in India ranging from 1.8% to 4.7%. Kulkarni SR et al [33] in his hospital based study in Maharashtra, reported that the prevalence of AMD was 1.38%, which is quite lower than what is reported in our study. Although true differences between the two studies in Maharashtra is possible, it is more likely that differences in examination techniques for the diagnosis of AMD led to the difference in prevalence. The previous study did not use retinal photographs to document AMD and hence may have underestimated early AMD.

In present study, it was found that prevalence of AMD was increasing as the age increases. Maximum prevalence of AMD was found in age group of ≥80 years (6.48%). The similar finding, about strong association of AMD with increasing age was found in all studies. [3,6,8,9,11,12,16,22,26,34]

In our study, we found that prevalence of AMD was 4.18% in smokers as compared with 1.89% in non-smokers. This was statistically highly significant. Gilles Chaine et al found that history of smoking was associated with AMD (OR=1.24). [22] Similar results were found in studies done by Klein R et al[15], Choudhury F et al, Kawasaki R et al, Krishnaiah et al, Chakravarthy et al.[12,11,6,26] A study by Shiraga et al[35] showed a dependent relation between number of cigarettes smoked and AMD; similarly, Vingerling et al[18] provided evidence for a dose-response relation between smoking and AMD, particularly for the neovascular form.

Delcourt C et al[17] found that an increased risk was present in participants who smoked more than 20 pack-years (OR = 3.0, 95% CI = 0.9-9.5 for 20-39 pack-years; OR = 5.2, 95% CI = 2.0-13.6 for 40 pack-years and more). In a study by Hyman et al[36], 83% of patients with AMD were smokers, in comparison with 65% in the control group.

In present study, we found that prevalence of AMD was highly significant in alcoholics as compared to non-alcoholics.

Shih-Jen Chen et al[25] in his study, found that wine drinking has been reported to be negatively associated with prevalence of any AMD, whereas heavy drinking is positively associated with early AMD.

Krishnaiah et al[6] found an inverse relationship between light alcohol consumption and prevalence of AMD. The prevalence of AMD was significantly lower in light alcohol drinkers (adjusted OR, 0.38; 95% CI, 0.19–0.76) compared with nondrinkers.

In this study, we found that prevalence of AMD was 3.9% in patients with history of cardiovascular disease as compared to 2.02% in patients without history of cardiovascular disease. (OR=1.96, 95% CI [1.21-3.06], p value =0.0020, highly significant).

Gilles Chaine et al found strong relation between coronary artery disease and advanced forms of AMD. [22] The OR was 3.30 with multivariate analysis in patients with GA; in patients with exudative disease the OR was 1.5. This association was suggested previously by Hyman et al in two reports.[36,37]

Chakravarthy et al[26] in his study: a systematic review and meta-analysis, a significant association was observed in the case control studies, with around double the odds of late AMD in individuals with cardiovascular disease (OR 2.20; 95% CI 1.48 - 3.26).

In our study, we found that prevalence of AMD was 8.19% in cataract operated patients as compared to 1.66% in patients not operated for cataract. This was statistically significant.

Our cross sectional study design does not allow us to assign causality and it is possible that some of the eyes with prior cataract surgery actually had AMD before the cataract surgery.

Gilles Chaine et al[22] conducted a case-control study to establish the role of previous cataract surgery as a risk factor of AMD. Both univariate and multivariate analysis found a significant relation between AMD and previous cataract surgery.

Krishnaiah et al[6] in his study found that prior cataract surgery was strongly associated with AMD in bivariate analysis (p<0.0001) and also in Multivariable Logistic Regression Analyses with Adjusted Odds Ratio (95% CI) = 3.79 (2.12–6.78).

Chakravarthy et al[26] in his systematic review and meta-analysis found that analysis of the prospective cohort studies showed that previous cataract surgery is a strong risk factor for neovascular AMD (RR 3.05; CI 2.05 - 4.55). This finding is supported by the results of the meta-analysis of the cross sectional studies (OR = 1.59; CI 1.08 - 2.34).

In a multivariable logistic regression model that adjusted for potential confounders, all the variables which were statistically significant in bivariate analysis were also statistically significant in multivariable logistic regression analyses with p value <0.0001. In this study, we found as the number of significant risk factors increases in individuals, the prevalence of AMD also increases.

CONCLUSION

We conclude that Prevalence of AMD was found to be 2.2%. Age was found to be strong, consistent & non-modifiable risk factor of AMD. Prevalence of AMD was significantly associated with severity of smoking as well as with severity of alcohol consumption. This study found that, as the number of risk factors increases in individuals, the prevalence of AMD also increases.

Three strong and consistent risk factors for AMD (i.e. Age, History of smoking and prior cataract surgery) and two significant and moderate risk factors for AMD (i.e. History of alcohol consumption and cardiovascular disease) were identified.

Conflict of interest-No.

REFERENCES

1. Brody BL, Gamst AC, Williams RA, Smith AR, Lau PW, Dolnak D, Rapaport MH, Kaplan RM, Brown SI. Depression, visual acuity, comorbidity, and disability associated with age-related macular degeneration. Ophthalmology. 2001;108:1893-1900.
2. Rovner BW, Casten RJ. Activity loss and depression in age-related macular degeneration. Am J Geriatr Psychiatry. 2002;10:305-310.
3. Friedman DS, O'Colmain BJ, Munoz B, Tomany SC, McCarty C, De Jong PT, Nemesure B, Mitchell P, Kempen J. Prevalence of age-related macular degeneration in the United States. Arch ophthalmol. 2004 Apr 1;122(4):564-72.
4. Resnikoff S., Pascolini D., Etya'ale D., Kocur I, Pararajasegaram R, Pokhrel GP,

Mariotti SP: Global data on visual impairment in the year 2002. Bull World Health Org 2004; 82:844-851.
5. Bird AC, Bressler NM, Bressler SB, Chisholm IH, Coscas G, Davis MD, de Jong PT, Klaver CC, Klein BE, Klein R. An international classification and grading system for age-related maculopathy and agerelated macular degeneration. The International ARM Epidemiological Study Group. Surv Ophthalmol. 1995;39:367–374.
6. Krishnaiah S, Das T, Nirmalan PK, Nutheti R, Shamanna BR, Rao GN, Thomas R. Risk factors for age-related macular degeneration: findings from the Andhra Pradesh eye disease study in South India. Investigative ophthalmology & visual science. 2005 Dec 1;46(12):4442-9.
7. Shrivastava RK, Jose R, Rammamoorthy K, Bhushan B, Tiwari AK, Malik KP. NPCB: Achievements and targets. NPCB India 2006;1:5-6
8. Leske MC, Wu SY, Hennis A, Nemesure B, Yang L, Hyman L, Schachat AP; Barbados Eye Studies Group. Nine-year incidence of age-related macular degeneration in the Barbados Eye Studies. Ophthalmology. 2006 Jan;113(1):29-35.
9. Wang JJ, Rochtchina E, Lee AJ, Chia EM, Smith W, Cumming RG, Mitchell P.Ten-year incidence and progression of age-related maculopathy: the blue Mountains Eye Study. Ophthalmology. 2007 Jan;114(1):92-8.
10. Augood CA, Vingerling JR, De Jong PT, Chakravarthy U, Seland J, Soubrane G, Tomazzoli L, Topouzis F, Bentham G, Rahu M, Vioque J. Prevalence of age-related maculopathy in older Europeans: the European Eye Study (EUREYE). Archives of ophthalmology. 2006 Apr 1;124(4):529-35.
11. Kawasaki R, Wang JJ, Ji GJ, Taylor B, Oizumi T, Daimon M, Kato T, Kawata S, Kayama T, Tano Y, Mitchell P. Prevalence and risk factors for age-related macular degeneration in an adult Japanese population: the Funagata study. Ophthalmology. 2008 Aug 1;115(8):1376-81.
12. Choudhury F, Varma R, McKean-Cowdin R, Klein R, Azen SP; Los Angeles Latino Eye Study Group. Risk factors for four-year incidence and progression of age-related macular degeneration: the los angeles latino eye study. Am J Ophthalmol. 2011 Sep;152(3):385-95.
13. McCarty CA, Dowrick A, Cameron J, McGrath B, Robman LD, Dimitrov P, Tikellis G, Nicolas C, McNeil J, Guymer R. Novel measures of cardiovascular health and its association with prevalence and progression of age-related macular degeneration: the CHARM Study. BMC Ophthalmol. 2008 Dec 22;8:25.
14. Varma R, Foong AW, Lai MY, Choudhury F, Klein R, Azen SP; Los Angeles Latino Eye Study Group. Four-year incidence and progression of age-related macular degeneration: the Los Angeles Latino Eye Study. (1997-2002) Am J Ophthalmol. 2010 May;149(5):741-51.
15. Klein R, Knudtson MD, Cruickshanks KJ, Klein BE. Further observations on the association between smoking and the long-term incidence and progression of age-related macular degeneration: the Beaver Dam Eye Study. (1988-1990) Arch Ophthalmol. 2008 Jan;126(1):115-21.
16. Delcourt C, Lacroux A, Carrière I, POLA Study Group. The three-year incidence of age-related macular degeneration: the "Pathologies Oculaires Liées à l'Age"(POLA) prospective study. American journal of ophthalmology. 2005 Nov 1;140(5):924-6.
17. Delcourt C, Diaz JL, Ponton-Sanchez A, Papoz L. Smoking and age-related macular degeneration. The POLA Study. Pathologies Oculaires Liées à l'Age. Arch Ophthalmol. 1998 Aug;116(8):1031-5.
18. Vingerling JR, Hofman A, Grobbee DE, de Jong PT. Age-related macular degeneration and smoking. The Rotterdam Study.(1990-1993) Arch Ophthalmol. 1996 Oct;114(10):1193-6.
19. Kawasaki R, Wang JJ, Aung T, Tan DT, Mitchell P, Sandar M, Saw SM, Wong TY; Singapore Malay Eye Study Group. Prevalence of age-related macular degeneration in a Malay population: the Singapore Malay Eye Study.(1992) Ophthalmology. 2008 Oct;115(10):1735-41.
20. Weiner DE, Tighiouart H, Reynolds R, Seddon JM. Kidney function, albuminuria and age-related macular degeneration in NHANES III(1998-1994). Nephrol Dial Transplant. 2011 Oct;26(10):3159-65.
21. Ajani UA, Christen WG, Manson JE, Glynn RJ, Schaumberg D, Buring JE, Hennekens CH. A prospective study of alcohol consumption and the risk of age-related macular degeneration. Ann Epidemiol. 1999 Apr;9(3):172-7.
22. Chaine G, Hullo A, Sahel J, Soubrane G, Espinasse-Berrod MA, Schutz D, Bourguignon C, Harpey C, Brault Y, Coste M, Moccatti D. Case-control study of the risk factors for age related macular degeneration. British Journal of Ophthalmology. 1998 Sep 1;82(9):996-1002.
23. Klein R, Klein BE, Wong TY, Tomany SC, Cruickshanks KJ. The association of cataract and cataract surgery with the long-term incidence of age-related maculopathy: The Beaver Dam Eye Study. Arch Ophthalmol. 2002;120:1551–1558.
24. Wang JJ, Klein R, Smith W, Klein BE, Tomany S, Mitchell P. Cataract surgery and the 5-year incidence of late-stage age-related maculopathy: pooled findings from the Beaver Dam and Blue Mountains eye studies. Ophthalmology. 2003;110:1960–1967.
25. Shih-Jen Chen, Ching-Yu Cheng, Kai-Ling Peng, An-Fei Li, Wen-Ming Hsu, Jorn-Hon Liu, and Pesus Chou. Prevalence and Associated Risk Factors of Age-Related Macular Degeneration in an Elderly Chinese Population in Taiwan: The Shihpai Eye Study. Invest Ophthalmol Vis Sci. 2008;49:3126–3133
26. Usha Chakravarthy, Tien Y Wong,Astrid Fletcher, Elisabeth Piault, Christopher Evans,Gergana Zlateva, Ronald Buggage, Andreas Pleil, Paul Mitchell. Clinical risk factors for age-related macular degeneration: a systematic review and meta-analysis. BMC Ophthalmology 2010;10:31
27. Epidemiology of age-related maculopathy (ARM)–epidemiologic review. John Hopkins University. vol.17 (2).
28. Rathod BLS, Chakravarti A, Manohar P. Age Related Macular Degeneration: AIOS CME SERIES (No. 23). ALL INDIA OPHTHALMOLOGICAL SOCIETY. 2011 April:12.
29. Maguire MG. Natural history of age-related macular degeneration. In: Berger JW, Fine SL, Maguire MG, eds. Age-Related Macular Degeneration. St. Louis: Mosby; 1999:17–30.
30. Hafron J, Mitra N, Dalbagni G, Bochner B, Herr H, Donat SM. Does body mass index affect survival of patients undergoing radical or partial cystectomy for bladder cancer? J Urol. 2005;173:1513–1517.
31. Vingerling JR, Dielemans I, Hofman A, Grobbee DE, Hijmering M, Kramer CFL, de Jong PTVM. Prevalence of age-related maculopathy in the Rotterdam Study. Ophthalmology 1995; 102:205-10.
32. Woo JH, Sanjay S, Au Eong KG. The epidemiology of age.related macular degeneration in the Indian subcontinent. Acta ophthalmologica. 2009 May;87(3):262-9.
33. Kulkarni SR, Aghashe SR, Khandekar RB, Deshpande MD. Prevalence and determinants of age-related macular degeneration in the 50 years and older population: a hospital based study in Maharashtra, India. Indian journal of ophthalmology. 2013 May;61(5):196.
34. Evans JR. Risk factors for age-related macular degeneration. Prog Retin Eye Res 2001; 20: 227–253.
35. Shiraga F, Matsuo N, Katayama S, Inoue Y, Tsuji T, Mihara M. Neovascular age-related macular degeneration. A case control study. Folia Ophthalmol Jpn 1987;38:525–33.
36. Hyman LG, Lilienfeld AM, Ferris FL, III, Fine SL. Senile macular degeneration: a case-control study. Am J Epidemiol. 1983;118:213–27.
37. Hyman L, He Q, Grimson R, Oden N, Schachat AP, Leske MC. Risk factors for age-related maculopathy. Invest Ophthalmol Vis Sci 1992; 33(suppl):801.