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Correlation study of modifiable risk factors and age related Maculopathy

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Abstract

Aim and Objective: To study relationship between ARMD and risk factors.

Methodology: A total sample size of 4000 patients above 60 years attending ophthalmology OPD of center were enrolled in the study. The data collection was done by using predesigned pretested questionnaire. A detailed history of selected subjects was recorded in relation to demographic information, family history, dietary habits, details of smoking and systemic problems, focused mainly on DM, hypertension and cardiac problems. All the patients selected for the study according to criteria for AMD subjected to detailed ocular examination with visual acuity; IOP measurement, slit Lamp biomicroscopy, direct and indirect ophthalmoscopic examination, Amsler grid test and fundus photography as needed.

Results and Conclusion: Age, occupation, smoking and co-morbidity with hypertension, diabetes mellitus, family history of AMD and cardiovascular disease showed statistical association with AMD. In the study; sex, place of living, education, socioeconomic status, diet, BMI, cataract surgery, lens opacity, iris colour and refractive error showed no statistically association with AMD.

Keywords: AMD, Risk Factors.

Introduction

Age related maculopathy (ARM) is a degenerative disorder of the central area of the retina (the macula) often associated with visual impairment which is more frequent after 60 years of age.[1]

The number of people affected by the disease is expected to rise due to increasing longevity. Development of adequate eye care for these patients should be based on knowledge about the prevalence of AMD. Further, preventive measures are the best strategy for any disease.[2]

The etiology of ARM is still unknown, despite intensive research on many fronts. The most prominent findings were an exponential increase in frequency with age, a significant familial and genetic component, and a strong association with smoking. Other risk factors that were found less consistently were atherosclerosis, low intake of antioxidant nutrients, and cataract extraction.[3]

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) are and not easily measured in routine clinical practice.[4-6] the skills required for an appropriate retinal evaluation to be performed followed by the interpretation of the severity of the signs to make a meaningful judgment of risk observed are limited to those with retinal specialty knowledge. Therefore, more precise estimates of risk for factors that could be accessed through routine history taking would be of value for appropriate treatment. Hence, the study was planned.

Material and Methods

The present study was cross sectional hospital based observational study undertaken to study relationship between ARMD and risk factor in patients >60 years of age attending OPD of Ophthalmology in tertiary care hospital over a period of 2 yrs. Sample size was calculated using 3% prevalence of pilot study.

Inclusion Criteria:

1. Patients age 60 years and above attending Ophthalmic OPD
2. Patients willing to participate in the study

Exclusion Criteria:

1. Cases with media opacity significant enough to preclude the maculopathy evaluation.
2. Patients not willing to participate
3. Patients having Pathological myopic degeneration, Central serous retinopathy, inherited central retinopathy, Toxic retinopathy, inflammatory maculopathy.

The study was approved by the Ethical Committee of the Medical College. Data was collected using Pretested questionnaire and after taking informed consent from the patient. Detailed information regarding demographic information, family history, dietary habits, details of smoking and systemic problems, focused mainly on DM, hypertension and cardiac problems was taken.

Present and best corrected distance visual acuity with Snellen chart was recorded in each eye. Intraocular pressure (IOP) was recorded in each eyes with help of Schiotz Tonometer. Eyes were examined for vision distortion with Amsler's grid chart. Pupillary dilation was achieved with 1% tropicamide after anterior segment biomicroscopy. Fundus was examined with Direct and Indirect Ophthalmoscope. Slit-lamp biomicroscopy (anterior and posterior) was done to evaluate macula using +90D lens. Findings on macula were recorded in detail Lens opacities observed on slit

lamp bimicroscopy were graded according to Lens Opacities Classification System III (LOCS III). Funds photography was undertaken with a fundus acquisition system (TRC 50 EX; Topcon) with preinstalled software (IMAGnet; Topcon) with high resolution camera (Nikon). Classification of AMD was done according to the international classification and grading system for age related maculopathy. Statistical analysis was done by bivariate analysis, using Chi Square Test and Fisher's Exact test.

Results

Prevalence of AMD in study population was 2.90%. Majority of patients were from age group 76-80 years (31.03%). The patients above 80 years were 22 (18.97%). The mean age among patients was 72.84±12.84 years. Majority of patients 51 (43.96%) belong to class V (B.G. Prasad classification). 22.41% patients were engaged as laborer. Among 116 patients, majority were primary schooling (40.51%). The patients with degree and above were only 12 (10.35%) while 19 (16.38%) patients were illiterate.

Table 1: Distribution of Patients according to age and sex

Age Group (years)	Male (%)	Female (%)	Total (%)
61-65	04 (07.27)	07 (11.48)	11 (09.48)
66-70	08 (14.55)	10 (16.39)	18 (15.52)
71-75	14 (25.45)	15 (24.59)	29 (25.00)
76-80	18 (32.73)	18 (29.51)	36 (31.03)
>80	11 (20.00)	11 (18.03)	22 (18.97)
Total	55 (100)	61 (100)	116 (100)

Table 2: Distribution of Patients according to WARMGS AMD Classification

Classification	No. of Patients	Percentage
Grade 1	69	59.48
Grade 2	27	23.27
Grade 3	17	14.66
Grade 4	03	02.59
Total	116	100

Table 3: Association between age and AMD

Age group (n)		Patients with AMD	P value	
61-65 (1643)		11	0.001*	
66-70 (1036)		18		
71-75 (784)		29		
76-80 (365)		36		
>80 (172)		22		
Total (4000)		116		
Sex (n)			0.45*	
Female (1760)		55		
Male (2240)		61		
Total (4000)		116		
Characteristics (n)		Patients with AMD	P value	OR(CI)
Place of living	Rural (2344)	68	0.93	1 (0.68-1.48)
	Urban (1656)	48		
Education	Illiterate (806)	19	0.30	0.77 (0.45-1.30)
	Literate (3194)	97		
Occupation	Manual (3382)	98	0.03*	1.17 (1.13-1.38)
	Non manual (618)	28		
SES	I, II, III (1277)	37	0.92	1 (0.66-1.52)
	IV & V (2732)	79		
Smoking	Present (634)	29	0.01*	1.81

	Absent (3366)	87		(1.15-2.83)
Alcohol consumption	Present (856)	27	0.47	1.17 (0.74-1.84)
	Absent (3144)	85		
Type of Diet	Vegetarian(2254)	74	0.12	0.73 (0.49-1.08)
	Mixed (1746)	42		
BMI	<18 (642)	10	0.06	1.01 (0.64-1.63)
	18-25 (2576)	93		
	>25 (782)	13		
Hypertension	Present (723)	42	<0.0001*	2.67 (1.78-4.00)
	Absent (3277)	74		
Diabetes Mellitus	Present (428)	27	<0.0001*	2.64 (1.65-4.18)
	Absent (3572)	89		
Family History of AMD	Present (32)	09	<0.0001*	14.12 (5.90-32.95)
	Absent (3968)	107		
Cardiovascular disease	Present (387)	18	0.03*	1.75 (1.01-3.00)
	Absent (3613)	98		
Cataract surgery	Present (872)	21	0.32*	0.79 (0.47-1.30)
	Absent (3128)	95		
Iris colour	Black/Brown (3615)	104	0.78*	1.09 (0.56-2.03)
	Blue/ grey (385)	12		
Refractive error	Present (982)	24	0.38*	0.80 (0.49-1.28)
	Absent (3018)	92		
Lens opacity	Present (1287)	31	0.20*	0.76 (0.49-1.18)
	Absent (2713)	85		

* P<0.05 statistically not significant

The majority of patients were observed with early AMD (97.41%). The patients with late AMD were 3 (2.59%). Table 2. Describes WARMGS AMD classification among the patients. The majority of patients were in Grade 1 (59.48%). The patients with AMD in Grade 2, 3 and 4 were 27 (23.27%), 17 (14.66%) and 03 (2.59%) respectively.

Table 3 showed association of various risk factors with AMD. Present study showed statistically association of AMD with increasing age (p<0.001). Sex of patient was not statistically associated with AMD. The prevalence of AMD among females was more but showed no significance. (OR=1.15; p=0.45)

Demographic characteristics such as place of living. (OR=1; p=0.93) education. (OR=0.77; p=0.30) socio economic status (OR=1; p=0.92) were not statistically associated with AMD. The association between occupation and AMD showed statistical significant. (OR=1.17; p=0.03) (P< 0.05)

Personal characteristics like smoking (P< 0.05) had statistically significant association with AMD. (OR=1.81; p=0.01), but alcohol consumption (OR=1.17; p=0.47) diet (OR=0.73; p=0.12 BMI (OR=1.01; p=0.06) were not statistically associated with AMD.

It was observed that patients with hypertension. (OR=2.67; p<0.0001), diabetes mellitus (OR=2.64; p<0.0001), family history of AMD (OR=14.12; p<0.0001), patients with cardiovascular disease (OR=1.75; p=0.03) had statistically significant association with AMD (P< 0.005)

History of cataract surgery (OR=0.79; p=0.32), Colour (OR=1.09; p=0.78) refractive error (OR=0.80; p=0.38), lens opacity (OR=0.76; p=0.20) were statistically not associated with AMD.

Discussion

The present cross sectional study was undertaken to see association of the risk factors associated with AMD. The study was conducted during the period of January 2014 to December 2015 in tertiary care center.

Prevalence of AMD in study population was 2.90%.various studies with similar prevalence were Jain et al.[7] (1984) (prevalence 4.7%), Gupta et al.[8] (2007) (prevalence 3.4%), Krishnaiah et al.[9] (2005) (prevalence 1.8%), Tromso study[10] (prevalence 3.5%) and European Eye Study[11] (prevalence 3.46%).

The prevalence of AMD was 2.45% among the males and 3.47% among the females. Similar findings were seen in study done by Krishna et al[12] with females (52%) prevalence. The findings of present study were in contrast to study done by Jagruti N. Vashi et al[13] where prevalence of AMD was more in males (1.54%) as compared to females (1.46%). The female gender to be associated with a greater prevalence of AMD, possibly confounded by longer life expectancy and increased health care utilization, others have revealed no gender differences in AMD risk.[14]

Majority of patients were from age group 76-80 years (31.03%). The patients above 80 years were 22 (18.97%). The ACES[15] had similar findings where,

age-specific prevalence of AMD was 1.3% for those aged 40– 49 years, 3.9% for those aged 50–59 years, 5.0% for those aged 60–69 years, and 6.9% for those aged >70 years. The findings were in contrast with the INDEYE[93] study, however, only found this association in late AMD, with prevalence rising from 0.4% in people aged 50–59 years to 4.6% in those aged >70 years. Krishna et al[(5)] showed 20% of the patients belong to lowest socioeconomic class.

Association of Various Risk Factors with AMD is seen in different studies. APEDS[(9)] reaffirmed age as a significant risk factor for AMD. In India, the study done by the APEDS[(9)] and also by the ACES[(15)] found no association between gender and AMD. The findings of the present study were in contrast with the study done by Jagruti N. Vashi et al;[(13)] where males had significantly higher risk for ARMD than females ($P < 0.005$). place of living was not associated with AMD in our study, The findings were in contrast with the Beijing eye study[(16)] which showed early ARM was statistically associated with living in a rural region ($p<0.001$).

In the study done by Klein et al[(17)] found incidence of early ARM was highest in those with less formal education. The association of early and late ARM with less education was also demonstrated in the AREDS[(18)] study and the EDCCS[(19)] demonstrated an association of less education with CNV. In another Chinese study, high educational background was a protective factor for AMD (OR: 0.76). A study by Klein et al[(17)] found strong association in early ARM was highest in those in the service industries and workers. Jagruti N. Vashi et al[(13)] showed significant association between occupation and ARMD ($P < 0.01$). In the Beaver Dam Eye Study, increased time spent outdoor in the summer was associated with a twofold increased risk of advanced AMD.[(20)]

In the present study it was observed that smoking had statistically significant association with AMD. (OR=1.81; p=0.01).

The findings were in accordance to study done by Jagruti N. Vashi et al[(13)] where smoking was significantly associated with ARMD ($P < 0.01$). Cigarette smoking is the significant risk factor identified in numerous studies.[(21-23)] Smoking doubles the risk of AMD and there appears to be a dose response whereby increasing odds are associated with an increased number of pack-years smoked.[(24)] Smoking is the major modifiable risk factor. Nicotine in general causes a lowering of antioxidants throughout body. It also compromises the immune system. Smoking cessation was associated with a reduced risk for AMD; the risk of developing AMD in those who had not smoked for over 20 years was comparable to the risk in nonsmokers.[(22)]

In the present study it was observed that alcohol consumption had no statistically significant association with AMD. (OR=1.17; p=0.47) Similar findings were seen in Chong EW et al,[(16)] Beaver Dam Eye Study.[(25)] BMI was not associated with AMD. Similar findings were also seen in study done by Jagruti N. Vashi et al[(13)] and Yasuda et al.[(18)] In a study by Age-related eye diseases study (AREDS) it was observed that persons with hypertension were 1.5 times more likely to have wet macular degeneration compared with persons without hypertension.[(16)] The findings were in contrast to study done by Jagruti N. Vashi et al[(13)] where they did not find an association between hypertension and ARMD ($P > 0.05$).

In the study by Clemons TE et al[(23)] the association had been made between diabetes and wet AMD in and found to be significant. But there is little evidence of an association with dry AMD. Diabetes may theoretically be a risk factor for AMD by influencing choroidal blood flow and increased plasma fibrinogen which may independently be associated with AMD.[(27)] The findings were in contrast to study done by Jagruti N. Vashi et al[(13)] where they did not find an association between DM and ARMD ($P > 0.05$).

In study done by Hyman LG et al[(12)] and Smith W. et al[(29)] by quantifying the influence of family history, with estimates of the odds ratio for a positive family history conferring risk of AMD ranging from 2 to 27. There is also strong support now for a genetic basis to AMD and ARM. The findings were in contrast to study done by Jagruti N. Vashi et al[(13)] where they did not find an association between family history of AMD and ARMD ($P > 0.05$).

In case-control study by Chaine G et al[(30)] there was a statistically significant association between coronary artery disease and AMD. The risk factors for cardiovascular disease (such as age, smoking, hypertension, hypercholesterolemia, post-menopausal estrogen use, diabetes, and dietary intake of fats, alcohol and antioxidants) have been associated with AMD in some studies. This raises the possibility that the causal pathways for cardiovascular disease and AMD may share similar risk factors.

In a study done by Jagruti N. Vashi et al[(82)] they did not find significant association between cataract surgery and ARMD ($P > 0.05$). The results were corroborating the study done in Maharashtra by Kulkarni et al[(31)] where no significant association between cataract surgery and ARMD.

In a study by Jagruti N. Vashi et al[(82)] it was observed that there is no significant association of ARMD with iris color ($P > 0.05$). A study by Frank et al. revealed that lighter iris is associated with a higher incidence of ARMD.[(32)]

The findings were in contrast with Weiter et al[(33)] who found that subjects with lightly and moderately pigmented irises were at higher risk of progression of AMD to late stages, in comparison with individuals with heavily pigmented irises.

It was observed that refractive error had no statistically significant association with AMD.

(OR=0.80; p=0.38) In AREDS, hyperopic refractive error was associated with both more extensive drusen and neovascular AMD.

In a strong cross-sectional study association was found between early age-related maculopathy (ARM) and nuclear opacity in the Beaver Dam Eye Study (OR, 1.96; 95% confidence interval, 1.28-3.01), nuclear opacity was not associated with the presence of late ARM at baseline or the 5-year incidence of early or late ARM or progression of ARM in that study.[17]

In Chesapeake Bay watermen, after controlling for age and other factors, there were significantly higher odds of AMD in the presence of nuclear opacity (OR=2.50; 95% confidence interval, 1.31-4.80) but not of cortical opacity.[34]

Conclusion

In the study, it was observed that age, occupation, smoking and co-morbidity with hypertension, diabetes mellitus, family history of AMD and cardiovascular disease showed statistically association with AMD.

In the study; sex, place of living, education, socioeconomic status, diet, BMI, cataract surgery, lens opacity, iris colour and refractive error showed no statistically association with AMD.

References

1. Young RW. Pathophysiology of age-related macular degeneration. Surv Ophthalmol 1987;31:291–305.
2. Resnikoff S, Pascolini D, Etya'ale D, Kocur I, Pararajasegaram R, Pokharel GP and Mariotti SP. Global data on visual impairment in the year 2002. Bull World Health Organ. 2004;82: 844–851.
3. Van Leeuwen R, Klaver CC, Vingerling JR, Hofman A, de Jong PT. Epidemiology of age-related maculopathy: a review. Eur J Epidemiol. 2003;18(9):845-54.
4. Chong EW, Kreis AJ, Wong TY, Simpson JA, Guymer RH: Dietary omega-3 fatty acid and fish intake in the primary prevention of age-related macular degeneration: a systematic review and meta-analysis. Arch Ophthalmol 2008,126:826-33.
5. Chong EW, Kreis AJ, Wong TY, Simpson JA, Guymer RH: Alcohol consumption and the risk of age-related macular degeneration: a systematic review and meta-analysis. Am J Ophthalmol 2008,145:707-15.
6. Seddon JM, Francis PJ, George S, Schultz DW, Rosner B, Klein ML: Association of CFH Y402H and LOC387715 A69S with progression of age-related macular degeneration. JAMA 2007,297:1793-800.
7. Jain IS, Prasad P, Gupta A, Ram J and Dhir SP (1984): Senile macular degeneration in northern India. Indian J Ophthalmol 32:343–346.
8. Gupta SK, Murthy GV, Morrison N, et al. Prevalence of early and late age-related macular degeneration in a rural population in northern India: the INDEYE feasibility study. Invest Ophthalmol Vis Sci. 2007;48(3):1007-1011.
9. Krishnaiah S, Das T, Nirmalan PK, et al. Risk factors for age-related macular degeneration: findings from the Andhra Pradesh eye disease study in South India. Invest Ophthalmol Vis Sci. 2005;46(12):4442–4449.
10. Erke MG, Bertelsen G, Peto T, Sjolie AK, Lindekleiv H, Njolstad I: Prevalence of Age related Macular Degeneration in Elderly Caucasians: The Tromso Eye Study. Ophthalmology 2012,119(9):1737-1743.
11. Augood CA, Vingerling JR, de Jong PT, Chakravarthy U, Seland J, Soubrane G, Tomazzoli L, Topouzis F, Bentham G, Rahu M et al: Prevalence of age-related maculopathy in older Europeans: the European Eye Study (EUREYE). Archives of ophthalmology 2006,124(4):529-535.21.
12. Tiruvengada Krishnan et al. Prevalence of Early and Late Age-Related Macular Degeneration in India: The INDEYE Study. IOVS, February 2010, Vol. 51, No. 2:701-707.
13. Jagruti N. Vashi, Kavita R. Bhatnagar, Renu M. Magdum, Akash P. Shah, Aman R. Khanna, Somil Jagani. Prevalence and risk factors of age-related macular degeneration in elderly patients. Sudanese Journal of Ophthalmology. 2015;7(1):1-5.
14. Ambati J, Ambati BK, Yoo SH, Ianchulev S and Adamis AP (2003): Age-related macular degeneration: aetiology, pathogenesis, and therapeutic strategies. Surv Ophthalmol 48:257–293.
15. Nirmalan PK, Katz J, Robin AL, et al. Prevalence of vitreoretinal disorders in a rural population of southern India: the Aravind Comprehensive Eye Study. Arch Ophthalmol. 2004;122(4):581–586.
16. Wu ZQ. Epidemiologic survey of senile macular degeneration. Chung Hua Yen Ko Tsa Chih 1992;28:246-7.
17. Klein, R, Klein, B. E, Jensen, S. C, and Moss, S. E. The relation of socioeconomic factors to the incidence of early age-related maculopathy: the Beaver Dam eye study. Am J Ophthalmol. 2001.132,128-31.
18. Risk factors associated with age-related macular degeneration. A case-control study in the age-related eye disease study: age-related eye disease study report Age-Related Eye Disease Study Research Group. Ophthalmology (2000).,107(3),2224-32.
19. Risk factors for neovascular age-related macular degeneration. The Eye Disease Case Control Study Group. Arch Ophthalmol (1992).,110, 1701-8.
20. Crruikshanks KJ, Klein R, Klein BE. Sunlight and age-related macular degeneration: The Beaver Dam Eye Study. Arch Ophthalmol 1993;111:514-8.
21. Thornton J, Edwards R, Mitchell P, Harrison RA, Buchan I, Kelly SP. Smoking and age related macular degeneration: A review of association. Eye 2005;19:935-44.
22. Khan JC, Thurlby DA, Shahid H, Clayton DG, Yates JR, Bradley M, et al. Smoking and age related macular degeneration: The number of pack years of cigarette smoking is a major determinant of risk for both geographic atrophy and choroidal neovascularization. Br J Ophthalmol 2006;90:75-80.
23. Seddon JM, George S, Rosner B. Cigarette smoking, fish consumption, omega-3 fatty acid intake, and association with age related macular degeneration: The US Twin Study of Age Related Macular Degeneration. Arch Ophthalmol 2006;124:995-1001.
24. Clemons TE, Milton RC, Klein R, Seddon JM, Ferris FL 3rd; Age-Related Eye Disease Study Research Group. Risk factors for the incidence of advanced age related macular degeneration in the Age Related Eye Disease Study (AREDS). AREDS report number 19. Ophthalmology 2005;112:533-9.
25. Moss SE, Klein R, Klein BE, et al. Alcohol consumption and the 5-year incidence of age-related maculopathy: the Beaver Dam eye study. Ophthalmology. 1998;105(5):789–94.

26. Yasuda M, Kiyohara Y, Hata Y, Arakawa S, Yonemoto K, Doi Y, et al. Nineyear incidence and risk factors for age related macular degeneration in a defined Japanese population the Hisayama study. Ophthalmology 2009;116:2135-40.
27. Smith, W, Mitchell, P, Leeder, S. R, and Wang, J. J. Plasma fibrinogen levels, other cardiovascular risk factors, and age-related maculopathy: the Blue Mountains Eye Study. Arch.Ophthalmol. (1998).,116,583-7.
28. Hyman LG, Lilienfeld AM, Ferris FL, et al. Senile macular degeneration: a case-control study. Am J Epidemiol. 1983;118:213–27.
29. Clemons TE, Milton RC, Klein R, Seddon JM, Ferris FL 3rd; Risk factors for the incidence of Advanced Age-Related Macular Degeneration in the Age-Related Eye Disease Study (AREDS) AREDS report no. 19. Ophthalmology. 2005 Apr; 112(4):533-9.
30. Chaine, G, Hullo, A, Sahel, J, Soubrane, G, Espinasse-berrod, M. A, Schutz, D, et al. Case-control study of the risk factors for age related macular degeneration. France-DMLA Study Group. Br. J Ophthalmol (1998).,82,996-1002.
31. Kulkarni SR, Aghashe SR, Khandekar RB, Deshpande MD. Prevalence and determinants of age related macular degeneration I n the 50 years and older population: A hospital based study in Maharashtra, India. Indian J Ophthalmol 2013;61:196-201.
32. Frank RN, Puklin JE, Stock C, Canter LA. Race, iris color, and age-related macular degeneration. Trans Am Opthalmol Soc 2000;98:109-15.
33. Weiter JJ, Delori FC, Wing GL, et al. The relationship of senile macular degeneration to ocular pigmentation. Am J Ophthalmol 1985;99:185–7.
34. West SK, Rosenthal FS, Bressler NM, et al. Exposure to sunlight and other risk factors for age-related macular degeneration. Arch Ophthalmol 1989;107:875–9.