TO EVALUATE THE RELATIONSHIP BETWEEN BODY MASS INDEX AND SERUM CHOLESTEROL IN AGE-RELATED MACULAR DEGENERATION (ARMD)

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ABSTRACT

Though it is known that age related macular degeneration is multi factorial, studies evaluating the relationship with obesity(BMI)and serum cholesterol are limited.166 individuals above 50 years age,[86 individuals having ARMD (GroupI) (with no other macular pathology) and 86 individuals as control (Group II), were included. A detailed history was recorded on a preset proforma and all the individuals underwent thorough posterior segment evaluation. Fund us Fluoresce in Angiography and Optical coherence tomography was done. ARMD was categorised according to AREDS classification. Body Mass Index (mass(kg) / (height(m))^2 was calculated and total serum cholesterol estimated in all individuals. Majority of individuals (55.23%) enrolled in study were aged 50-60 years. Males (54.65%) outnumbered females (43.35%).Proportion of individuals having normal BMI was higher in Group II (73.26%) as compared to Group I (47.67%) and this difference was found to be statistically significant. Proportion of individuals with borderline high serum cholesterol and high serum cholesterol was higher in Group I as compared to Group II(p). Of the risk factors evaluated a statistically significant association was seen with abnormal BMI (<18.6 or >25.1 kg/m^2) (p=0.003) and high Serum cholesterol (p=0.009). Higher proportion of individuals with abnormal BMI were suffering from Advance AMD (92.31%) as compared to Intermediate AMD (66.67%) and Early AMD (42.19%). Similarly, higher proportion of individuals with raised S. Cholesterol were suffering from Advance AMD (69.23%) and Intermediate AMD (55.56%) as compared to Early AMD (28.13%). Increased BMI (>25 kg/m^2) and serum cholesterol levels are significant risk factors for ARMD. Increasing BMI and S. cholesterol levels have a significant directly proportional association with progression and advancement of ARMD.

KEYWORDS: Age-Related Macular Degeneration, Body Mass Index, Serum Cholesterol.

INTRODUCTION

Age related macular degeneration (ARMD) is a common, chronic, progressive degenerative disorder of the macula that affects older individuals and features central visual loss as a result of drusen deposition, geographical atrophy, serous detachment of the retinal pigment epithelium, and neovascularization [1]. The disease is thought to be caused by a combination of genetic and environmental factors, and is common in people over fifty years of age. Age-related macular degeneration has a significantly negative impact in affected people [2-4] because it usually affects an eye where vision is already compromised and is deteriorating due to age related co-association of multiple coexisting ocular or systemic diseases. Age-related macular degeneration (ARMD) is the third leading cause of blindness and accounts for 8.7% of the world population (2012) [5]. ARMD has been found to be second only to cataract as the cause of severe visual loss in Asian countries. Epidemiological studies of age related macular degeneration (ARMD) have mostly been done in industrialized nations. There have not been many studies with regards to the epidemiology of this disease in India. Age-related macular degeneration may emerge as a major public health problem in India as well, with increasing life expectancy [6]. Various treatment modalities for ARMD are effective only in the early clinical stages. Early detection of ARMD with accuracy can be possible by study and knowledge of risk factors for ARMD coupled with investigations. Hence The present study was carried out with the aim to study BMI and cholesterol as a risk factors likely to contribute to occurrence of age-related macular degeneration.

Material and methods: In this observational, cross sectional study of 166 patients. 86 patients of ARMD with no other macular pathology group (as cases) and 86 normal individuals ≥50 years having no macular pathology group (as control), regardless of sex, were invited to participate in the study. Informed consent was obtained from all the participants before including them in the study. The study protocol was in accordance with the Declaration of Helsinki and was approved by our institutional research board.

The present study was conducted in the Department of Ophthalmology in tertiary hospital in North India. The individuals with opaque media making fundus visualization difficult, having any other macular pathology, terminally ill patients or those having a prolonged stay at hospital/ nursing home, patients not willing to participate in the study were excluded from the study. A detailed history about symptoms and the risk factors was recorded on a preset proforma and all the individuals underwent Visual Acuity assessment (Snellen's chart), Amsler grid and Fundus Examination by Direct & Indirect ophthalmoscopy. Specialised investigations included Fund us Fluoresce in Angiography(carl-zeiss NMFA) and Optical coherence tomography(Cirrus 500 machine) were performed as and when needed. ARMD was categorised according to AREDS classification.(No AMD, Early, Intermediate and Advanced AMD). Body Mass Index (mass(kg) / $(\text{height(m)})^2$ was calculated and serum cholesterol was estimated. Body mass index[7] was categorised as underweight (<18.5), normal (18.5 to 25), overweight (25 to 30) and obese (>30).Total serum cholesterol estimation (mg/dl) [8] –as desirable (<200),borderline high (200-239),high(>239).

Statistical analysis were performed using commercially available statistical software package (SPSS software for Windows Version 15.0,SPSS,Chicago,IL,USA).Univariate categorical analyses were performed using Student's t-tests and Pearson's Chi square tests, and a P-value of <0.05 was considered statistically significant.

Results: A total of 86 individuals of ARMD (Group I) and 86 normal individuals having no macular pathology (Group II) aged ≥50 years, regardless of sex, were enrolled in the study.

Majority of (55.23%) enrolled in study were aged 50-60 years. Though higher proportion of individuals aged 50-60 were found in Group II (56.98%) as compared to Group I (53.49%) but this difference was not found to be statistically significant (p=0.534).[Table 1]

Males (54.65%) outnumbered females (43.35%). Though higher proportion of males were present in Group I (58.14%) as compared to Group II (51.16%) but this difference was not found to be statistically significant (p=0.358).[Table 1]

Overall 58.72% of individuals were from rural background. Though proportion of rural population in Group II (62.79%) was higher than that of Group I (54.65%) but this difference was not found to be statistically significant (p=0.278).

Major of study population preferred Vegetarian (51.74%) diet. Though proportion of individuals preferring vegetarian diet was higher in Group II (53.49%) as compared to Group I (50.00%) but this difference was not found to be statistically significant (p=0.647).

The only addiction found in individuals of present study was for tobacco. Smoking was prevalent in 20.93% of study population. Habit of tobacco chewing was more prevalent (39.53%) as compared to smoking(20.93%). In either type of addictions the difference in duration of tobacco chewing or smoking in the two groups was not found to be statistically significant (p=0.430).

Majority of the individuals, in either group, were indoor workers with no direct exposure to sunlight conditions. Though higher proportion of individuals of Group II (77.91%) as compared to Group I (67.44%) were exposed to indoor sunlight conditions but this difference was not found to be statistically significant (p=0.124). None of the individuals enrolled in the study reported known family history of ARMD. Proportion of individuals having normal BMI was higher in Group II (73.26%) as compared to Group I (47.67%) and this difference was found to be statistically significant.[Table 2]

In majority of individuals of study population (76.16%) serum cholesterol was found to be within desirable limits. Proportion of individuals with borderline high serum cholesterol and high serum cholesterol was higher in Group I as compared to Group II and this difference was found to be statistically significant.[Table 3] .Of the above risk factors a statistically significant association was seen with abnormal BMI (<18.6 or >25.1 kg/m^2) (p=0.003) and high Serum cholesterol only (p=0.009).

Higher proportion of individuals with abnormal BMI were suffering from Advance ED (92.31%) as compared to Intermediate AMD (66.67%) and Early AMD (42.19%).Similarly, higher proportion individuals with raised S. cholesterol were suffering from Advance ED (69.23%) and Intermediate AMD (55.56%) as compared to Early AMD (28.13%).

Discussion:

AMD is the leading cause of visual deterioration and legal blindness in patients over 60 years of age [9]. The loss of central vision and high-resolution visual acuity from untreated AMD can lead to an irreversible vision loss in the form of loss of reading, facial recognition, and driving [10].

In the present study, attempt has been made to study age-related macular degeneration in general population of individuals aged 50 years and above and to study various risk factors contributing to occurrence of age-related macular degeneration. An attempt was also made to explore the possible relationship of BMI and cholesterol with the clinical type of ARMD.

One of the reasons for lower frequency of ARMD patients aged above 60 years was also due to the strict selection criteria used in the present study. In present study, we excluded terminally ill patients and those having a prolonged stay at hospital/nursing home and those having other macular pathologies. Both these factors selectively contributed towards non inclusion of a major group of older age cases. It has been seen that with increasing age, the burden of chronic illnesses and prolongation of hospital stay increases and hence affected the age related general trend of ARMD [11].

Majority of individuals with ARMD (Group I) were males (58.14%). There were 41.86% females. Male to female ratio was 1.4:1 (Table 1). In some studies, female gender has been considered as a weak risk factor with inconsistent association for late age-related macular degeneration [12,13]. In contrast some studies have indicated a higher risk in women as compared to men [14]. However, meta-analytical data show no such gender related difference in prevalence rate [15]. The lower proportion of females in present study might be owing to difference in gender related health seeking behaviour.

Majority of individuals with ARMD were from rural areas (54.65%). There were only 45.35% individuals from urban areas (Table 1). The reason for this is in the fact that our facility is located in a semi urban area and the large proportion of rural individuals availing our facility.

We did not find an association between diet and ARMD. Almost half the individuals in both cases as well as controls were vegetarian. Non-vegetarian diet had slightly increased odds of ARMD (OR=1.15; 95% CI=0.632-2.092) (Table 1). Kulkarni *et al.* (2013) tried to evaluate the impact of vegetarian and non-vegetarian diet on macular disorder but did not report any significant association [16]. This is in consistence with the findings of present study. A number of other studies have evaluated the association between diet and ARMD, but most of them have focussed on the fat levels and glycemic index of diet rather than focussing on the vegetarian and non-vegetarian type of diet [17]. The progression of early AMD is accelerated by high-fat intake, whether saturated, monounsaturated, polyunsaturated, or trans unsaturated [18] and reduced by a low intake of saturated fat [19]. Nuts and fish also reduced the risk of progression [19].

An attempt was made to evaluate the role of personal addictions and habits as a risk factor for ARMD. Majority in both the groups were non-smokers and non-tobacco users. In both the groups, no significant association of ARMD with duration of tobacco use and smoking habit was observed. Studies have indicated a strong association between smoking habit and age related macular disorders [20,21]. This difference between findings of present study and that of those reported in literature could be attributed to difference in size of studies. Most of the studies reporting an association between smoking habits and age related macular disorders have evaluated the prevalence of ARMD in larger sample size and had evaluated the risk in terms of current smokers/ever smokers and non-smokers. In present study, we focussed mainly on the duration of smoking. Despite having observed a high prevalence of non-smokers among controls (83.72%) as compared to cases (74.42%) (Table 3), we did not find a statistically significant association either between duration of smoking or smoking habit alone (OR=1.77; 95% CI 0.835-3.742). With regards to any association of use of smokeless tobacco (tobacco chewing) with ARMD, no study was found in available literature. In present study, we investigated this relationship but did not find a significant association and found minor higher odds (OR=1.22; 95% CI 0.659-2.241).

We did not find a significant association between exposure to sunlight and ARMD. Majority of cases as well as controls had an indoor profile and had limited outdoor sunlight exposure. In the present study we noticed the sun exposure and found a positive history of outdoor sunlight exposure in 28 (32.56%) of cases as compared to 19 (22.09%) of controls (Table 4) yet none of the subjects either amongst cases or controls had a direct sunlight exposure above 8 hours per day and despite having higher odds (OR=1.70; 95% CI=0.862-3.362), this relationship could not be proven statistically. The absence of family history in any case in present study might be attributed to one of the undiagnosed or unattended problems owing to lack of awareness and adequate healthcare facilities.

We found prevalence of patients with higher BMI was significantly higher in ARMD cases as compared to controls (p=0.002) (Table 2). Similarly serum cholesterol levels of ARMD cases were also high as compared to that of controls (p<0.001) (Table 3). These findings indicated a high affinity of ARMD with fat accumulation and lipid levels. Like other controversial relationships of ARMD with different risk factors, these also have a limited validity and conflicting reports in literature. Adams *et al.* (2011) in their study in a cohort of 21287 patients found a positive association between abdominal obesity and risk of ARMD in men but found a reverse relationship for same parameters in women [22]. Peeters *et al.* (2008) have studied the problem with a different perspective and showed that a 3% or more decrease in Waist hip ratio was associated with 29% lower odds of any ARMD [23]. Nominally high odds of developing ARMD over a five-year incidence evaluation were also established by Jonasson *et al.* (2014) who also showed the odds of ARMD to be 1.62 times higher among those having raised cholesterol levels [24]. However, Hymen *et al.* (2000) did not show a significant association between cholesterol levels and ARMD for a 10-year prospective evaluation[25].

Another study by Seddon *et al* . (2003) has discussed the obesity using different approaches – *i.e.* BMI, waist circumference and waist-hip ratio [26]. In their study relative risk (RR) was 2.35 (95% confidence interval [CI], 1.27-4.34) for a body mass index of at least 30, and 2.32 (95% CI, 1.32-4.07) for a body mass index of 25 to 29, relative to the lowest category (<25) after controlling for other factors (P =.007 for trend). Higher waist circumference was associated with a 2-fold increased risk for progression (RR for the highest tertile compared with the lowest, 2.04; 95% CI, 1.12-3.72), with a significant trend for increasing risk with a greater waist circumference (P =.02). Higher waist-hip ratio also increased the risk for progression (RR, 1.84; 95% CI, 1.07-3.15) for the highest tertile compared with lowest (P =.02 for trend). A similar relationship was also observed by Clemons *et al.* (2005) [27]. Thus, most of the studies in literature support the view that obesity either in terms of abdominal obesity or in terms of BMI have a positive association with ARMD and do not have much controversy as for other issues. Although Hyman *et al.* (2000) [25] and Klein *et al.* (2010) [28] ruled out an association of cholesterol with ARMD, this association has been established in other studies [29,30,31]. This conflicting relationship has been addressed by some workers by establishing the association of different types of cholesterol (particularly increased HDL levels) with ARMD [30-32]. Unfortunately, we did focus only on total cholesterol levels and hence are not in a position to comment on this. Majority of patients were early AMD patients (n=64; 74.4%) followed by those with advanced AMD (n=13; 15.1%) and then intermediate AMD (n=9; 10.5%) (Table 4).

A varied nature of relationship with different risk factors was observed for different parameters, abnormal BMI was seen to be higher in intermediate (66.7%) and advanced AMD (92.31%) as compared to early AMD (42.19%) (p=0.003; χ^2 for trend) .These findings are in agreement with the observations made by Seddon *et al.* (2003) who observed higher body mass index as a risk for progression to the advanced forms of AMD [33]. Raised S. cholesterol was also found to be significantly more common in intermediate and advanced stages (55.56% and 69.23% respectively) (p=0.009; χ^2 for trend) . With respect to prevalence of higher stages of ARMD with increasing cholesterol level, Friedman (2000) and Curcio *et al.* (2001) provided a reasonable explanation for association of atherosclerosis with late stages of AMD through its effect on the choroidal circulation and possible deposition of lipids in the Bruch's membrane [34,35].

The findings in present study once again established that age is the biggest risk factor for age-related macular degeneration and it is often associated with a number of events taking place with the progression of age. we established BMI and cholesterol levels to be carrying not only a higher risk of ARMD but to be also associated with higher severity of ARMD, however, given the polymorphic nature of relationships of ARMD in different studies, this is another finding that needs further evaluation and assessment at community level.

Diabetes, hypertension and hyperopic refraction are some age-related problems and their role in causation of ARMD must be evaluated with a carefully planned study [36,37,38].

Conclusion

The present study is path breaking in several ways as it challenges and questions the validity of several traditionally mooted risk factors for ARMD. However, at the same time it questions and highlights the issue of confounding role of different factors such as lifestyle disorders that incidentally also have a relationship with increasing age. The present study, thus not confounds the issue of risk factors of ARMD but tries to clear up the issue with a renewed perspective and an open-mind approach. Further elaboration on the issue is much issue of risk factors of ARMD but tries to clear up the issue with a renewed perspective and an open-mind approach. Further elaboration on the issue is much demanded.

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DECLARATION OF CONFLICTING INTERESTS

None declared.

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TABLE 1-Demographical Profile of Study Population

	No.	%	No.	%	No.	%
Age Group (yrs)						
50-60	46	53.49	49	56.98	95	55.23
61-70	31	36.05	32	37.21	63	36.63
>=71	9	10.47	5	5.81	14	8.14
	χ^2=1.253 (df=2); p=0.534					
Gender						
Male	50	58.14	44	51.16	94	54.65
Female	36	41.86	42	48.84	78	45.35
	χ^2=0.845 (df=1); p=0.358					
Habitat						
Rural	47	54.65	54	62.79	101	58.72
Urban	39	45.35	32	37.21	71	41.28
	χ^2=1.175 (df=1); p=0.278					
Diet						
Vegetarian	43	50.00	46	53.49	89	51.74
Non-vegetarian	43	50.00	40	46.51	83	48.26
	χ^2=0.210 (df=1); p=0.647					

Table-2 ARMD profile in comparison to Body Mass Index

	Group I (ARMD) (n=86)		Group II (Controls) (n=86)		Total	
	No.	%	No.	%	No.	%
BMI (Kg/,m^2)						
16.1-18.5: Underweight	3	3.49	0	0.00	3	1.74
18.6-25: Normal	41	47.67	63	73.26	104	60.47
25.1-30 : Overwt	31	36.05	22	25.58	53	30.81
30.1-35: Obese Cl I	10	11.63	1		11	6.40
>=40.1: Obese Cl 3	1	1.16	0	0.00	1	0.58
	χ^2=17.546 (df=4); p=0.002					

Table-3: ARMD profile in comparison to Serum Cholesterol

	Group I (ARMD) (n=86)		Group II (Controls) (n=86)		Total	
	No.	%	No.	%	No.	%
Serum Cholesterol						
Desirable (<200)	54	62.79	77	89.53	131	76.16
Borderline high (200-239)	25	29.07	9	10.47	34	19.77
High (>239)	7	8.14	0	0.00	7	4.07
	χ^2=-18.568 (df=2); p<0.001					

Table-4. Association of Abnormal BMI with ARMD

	Early AMD (64)		Intermediate AMD (n=9)		Advanced AMD (n=13)		Total (n=86)		Statistical Significance	
	No.	%	No.	%	No.	%	No.	%	χ^2	'p'
Abnormal BMI	27	42.19	6	66.67	12	92.31	45	52.33	11.709	0.003