Frequency of ARMD in the Local Pakistani Population Presenting at a Tertiary Care Hospital

Hussain Ahmad Khaqan, Usman Imtiaz, Hassan Raza, Umrah Imran, Ateeq-ur-Rehman

. . . .

See end of article for authors affiliations

…..…………………..

Correspondence to:
Dr. Hussain Ahmad Khaqan
FRCS Associate Professor
Department of Ophthalmology
Lahore General Hospital

Purpose: To evaluate the frequency of ARMD in local Pakistan population presenting at a tertiary care hospital.

Study Design: Cross sectional descriptive study.

Place and Duration of Study: Lahore General Hospital from 1st October 2015 to30[th] March 2018.

Material and Methods: A total of 1002 participants with age above 65 years were included. Participants with clear ocular media were selected randomly from outpatient department. Informed consent was taken from all participants for taking retinal images. A non-mydriatic 8 megapixel (MP) Topcon fundus camera was used to take 45 degree retinal images. Fundus fluorescein angiography was done in patients having ARMD and they were treated accordingly. A proforma was designed to collect data including age, sex, smoking, far and near vision and status of retina (ARMD present or not and its type). Blood pressure, serum cholesterol, weight, and height of persons having ARMD were recorded.

Results: A total of 1020 participants were included in study. There were 500 (49%) males and 520 (51%) females. Mean age of participants was 70.3±5 years. Frequency of ARMD was found to be 1.56% in local population. Prevalence of dry ARMD (68.75%) was greater than wet ARMD (31.25%). There was no significant gender predisposition for ARMD. Among all risk factors of ARMD smoking (41%) had strong association while hypertention (24%), diabetes (12%), hyperlipidemia (15%) and obesity (9%) had also some association with ARMD.

Conclusion: Age related macular degeneration is most frequent in smokers and they should be educated about this risk.

Keywords: Age-Related Macular Degeneration, Hypertension, Diabetes, Obesity.

…..…………………..

A ge Related Macular Degeneration (ARMD) is one of the leading causes of blindness worldwide[1]. It is a chronic disease that affects the part of retina, which is required for maximum fine details of vision. According to an analysis 15 million people are affected with ARMD in North America[2]. Worldwide its documented prevalence is 5.6%[3].

Age is one of the primary risk factors for ARMD, others include smoking, obesity, hypertension, hypercholesterolemia, excessive sun exposure and a diet deficient in fruits and vegetables[4]. There are two documented types of ARMD i.e. Dry and Wet ARMD (neovascular). Dry form is more prevalent than wet ARMD but gross vision loss is associated with wet form of ARMD[2]. ARMD can also be classified on the

grounds of severity i.e. early, intermediate and advanced ARMD[5]. Small to intermediate size drusens with no pigmentation are seen in early ARMD while intermediate ARMD includes several intermediate size drusen with at least one large size drusen (> 125 um)[5]. Geographic atrophy and exudative ARMD are considered as advanced forms of ARMD[5]. Symptoms of dry ARMD appear gradually and are usually associated with difficulty in adaptation to light or dark while wet ARMD is associated with profound loss of central vision and metamophopsia[6].

There are many treatment modalities for wet ARMD including intra-vitreal Anti VEGF, intra-vitreal steroid, Laser photocoagulation and Photodynamic therapy[7]. Dry ARMD does not have specific treatment but includes prophylaxis and visual rehabilitation[8]. Anti oxidants and zinc supplements have an important role in preventing ARMD in other eye[9]. These supplements are referred as "AREDS" supplements because their efficacy was established by the National Eye Institute's Age-Related Eye Disease Study[9]. Trials of other supplements i.e Leutin, xiazanthine and omega-3 fatty acids are in progression of ARMD[10]. The purpose of our study was to find the frequency of ARMD in a tertiary hospital and also determine associations with other conditions.

MATERIAL AND METHODS

A total of 1020 participants with age above 65 years were included in the study. Participants with clear ocular media were selected randomly from outpatient department. Informed consent was taken from all participants for taking retinal images. Distance visual acuity was recorded by using Snellen's acuity chart while near vision was recorded by using Jaegar near vision chart. A non-mydriatic 8 MP Topcon fundus camera was used to take 45 degree retinal images. Fundus fluorescein angiography was done in patients having ARMD and treated accordingly. A proforma was designed to collect data including age, gender, status of retina (ARMD present or not) and smoking. All images and data were collected by the same person.

Associations of ARMD i.e. smoking, hyperlipidemia, hypertension, diabetes and obesity were also evaluated. Patients with known history of hypertension and those with blood pressure of > 150/90 mm Hg were labeled as hypertensive. Patients with known history of diabetes and those with fasting blood sugar level of > 7 mmol were considered as diabetics. Participants with fasting lipid profile more than 250 mg/dl were considered hyperlipidemic. Height and weight were measured. Body mass index was calculated using the formula: weight (in KGs)/(height × height) (in meters).

ARMD was graded according to international classification. Digital fundus photography was done including colored as well as red free images. Dry ARMD included drusens and geographic atrophy with respect to severity of disease. Wet ARMD included disorders of choriocapillary plexus including choroidal neovascular membranes (CNVM) and pigment epithelial detachment (PED).

We assumed that the proportion of ARMD would be 5.6% according to a published study[4]. To achieve 95% confidence interval with acceptable error margin of 3%, we needed to examine 1020 persons of this age group. Statistical analysis was done by SPSS version 20.

RESULTS

A total of 1020 participants were included in this study. There were 500 (49%) males and 520 (51%) females. Mean age of participants was 70.3 ±5 years. Frequency of ARMD came out to be 1.56% (16/1000) in local population. Prevalence of dry ARMD (68.75%) was greater than wet ARMD (31.25%). There was no significant gender predisposition for ARMD. Age wise statistical analysis is shown in Table 1.

Table 1: Age-wise distribution of ARMD in local population.

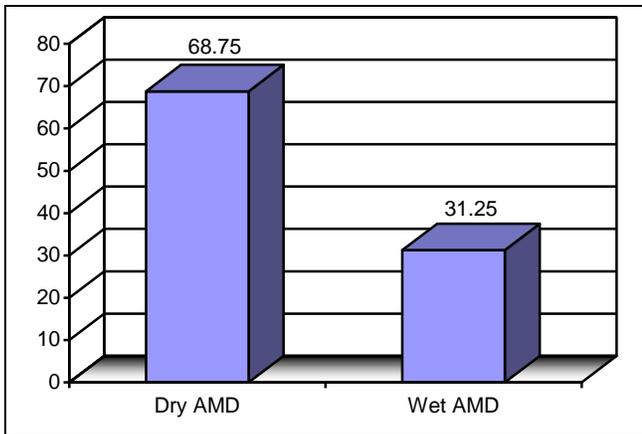| Age Groups	No. of Persons (n)	Percentage %	ARMD (X)	Percentage ARMD %
60 – 65	550	53.92	3	0.29
66 – 70	300	29.41	6	0.58
71 – 75	150	14.7	4	0.39
75 – 80	20	1.96	3	0.29

Fig. 1: Percentage of Dry VS Wet ARMD.

Associations of ARMD i.e. smoking, hyperlipidemia, hypertension and obesity were also evaluated. Among all risk factors of ARMD smoking (41%) had the strongest association while hypertension (24%), hyperlipidemia (15%), diabetes (12%) and obesity (9%) had also some association with ARMD. (Fig 02)
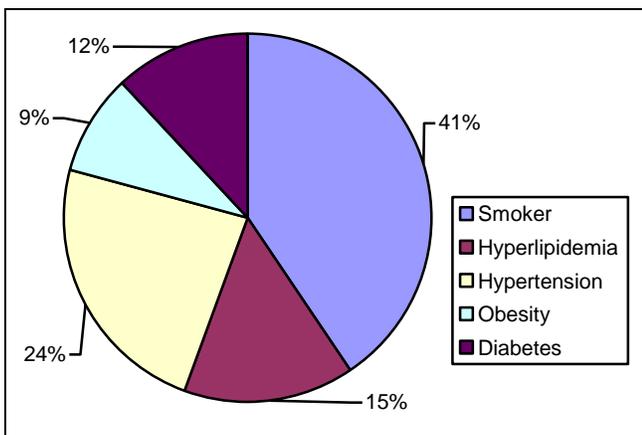

Fig. 2: Risk factors for ARMD.

DISCUSSION

Age related macular degeneration (ARMD) is one of the leading causes of acquired blindness worldwide[11]. In our study its prevalence came out to be 1.56%, which is quite lower than USA, which is 5.6%[3]. Another study was conducted in India showing prevalence near to our study[12]. Novartis Pharmaceuticals UK also suggested 26,000 new cases of wet AMD in the UK per year, reported as being calculated from our earlier review of prevalence. This figure is commensurate with estimates that there are 13,000 to 37,000 incident cases of neovascular AMD in England and Wales per year[13].

A study was conducted to evaluate the difference in prevalence of ARMD among black and white races; they concluded no significant difference among these races with respect to prevalence rate. Mediums size drusen were found equally in both races but in white race they transformed to large size drusen later more frequently[14]. Equal proportion of male and female were included in the study but there was no gender predisposition for ARMD. There are many studies which showed the same pattern of gender predisposition[15]. Another study showed that females are more prone to develop neovascular AMD than males and associated with profound visual loss[16]. Focal hyper-pigmentation was also evaluated in our study and found in only 5 patients (3 female and 2 male). A study conducted in Baltimore suggested that focal hyper pigmentation was more prevalent among white race as compared with black race people[17].

A study was conducted in Brazil among Japanese immigrants and they showed that ARMD was more prevalent in men while in our study no such difference was noted. Maximum age group prone to ARMD was 60-65 years of age group while in our study it came out to be 66-70 years of age group[18]. Another study showed that 66-70 years of age group is most prone to develop ARMD, which is same as our study[19]. In our study we observed that dry ARMD was more prevalent (68.75%) than wet ARMD (31.25%). These results are consistent with published studies[29,30]. In contrast a study was published in UK showed that there is no significant difference of prevalence among dry and wet ARMD[20].

Dry ARMD is associated with gradual loss of vision while wet ARMD is associated with sudden gross loss of vision[12,13]. In our study, patients with wet ARMD were associated with gross drop in vision as compared with dry ARMD. Dry ARMD if not treated can lead to wet form of ARMD (CNV or PED). Etiology of ARMD is not well known but there are few documented predisposing factors i.e. smoking, hypertension, hyperlipidemia, diabetes and obesity which my lead to ARMD[4]. In our study smoking was the most significant predisposing factor. According to a survey in USA smoking and hyperlipidemia were among the most significant predisposing factors for developing ARMD[21]. Body mass index is also an important predisposing factor for developing ARMD but no association of high BMI was seen in our study.

There are some psychological issues like depression that may predispose to ARMD as well[22]. Studies show that greater attention from families, physicians, and society to the mental health needs and also alleviation of mobility challenges may help improve the condition[22].

Our study showed hypertension as the second significant predisposing factor for ARMD. There are multiple studies showing relation of hypertension with ARMD[17,22]. A study was conducted that showed that antihypertensive drugs like systemic beta blockers reduce lysozyme levels. These drugs reduce the requirement for intravitreal anti-VEGF injections in patients with wet AMD[23].

As there are few treatment options for the management of ARMD so its prevention and retardation of growth plays an important role. AREDS study was conducted to evaluate the role of antioxidants in prevention and delaying the disease process. AREDS explained that antioxidants i.e. Beta carotene (15 mg), Vitamin C (500 mg), Vitamin E (400 IU), Zinc (80 mg) and copper (as cupric oxide) are associated with remarkable delay in progression of disease[24].

Another clinical trial AREDS 2 was carried out to look for efficacy of omega 3 fatty acids and Lutein/Zeaxanthin in reducing the rate of progression of disease. AREDS 2 clinical trial explained that Omega 3 fatty acids are of no importance when added with these supplements while lutein and zeaxanthin was associated with delay in progression of ARMD. Beta carotene was found to be associated with increased risk of lung cancer[25]. In this study 50% of patients were smoker while in our study 40% of patients were smoker. According to different published studies smoking came out to be the most persistent risk factor in addition to all other risk factors.

As there is no such geographic data published regarding the prevalence and incidence of age related macular degeneration in Pakistan so this will help to compare it with other populations in East as well as in Western countries. This evidence-based data can be used to provide health care and social awareness to population and its comparison with other parts of the world. This awareness can help to prevent further by following the international guidelines that will help in present as well as in future.

CONCLUSION

Age related macular degeneration is most frequent in smokers and they should be educated about this.

Author's Affiliation

Dr. Hussain Ahmad Khaqan
FRCS Associate Professor
Department of Ophthalmology
Lahore General Hospital

Dr. Usman Imtiaz
FCPS, Vitreo-retina fellow
Department of Ophthalmology
Lahore General Hospital

Dr. Hassan Raza
MRCSED, Final year PGR
Department of Ophthalmology
Lahore General Hospital

Dr. Umrah Imran
MBBS, Final year PGR
Department of Ophthalmology
Lahore General Hospital

Dr. Ateeq-ur-Rehman
MBBS, 2nd year PGR
Department of Ophthalmology
Lahore General Hospital

Role of Authors

Dr. Hussain Ahmad Khaqan
Conception and Design, Literature Search

Dr. Usman Imtiaz
Literature Search, Critical Review, Manuscript editing

Dr. Hassan Raza
Data Collection, Manuscript writing

Dr. Umrah Imran
Data Collection, Manuscript writing

Dr. Ateeq-ur-Rehman
Data Analysis, Data Collection, Literature Search

REFERENCES

1. **Klein R, Klein BE, Linton KL.** Prevalence of age-related maculopathy: The Beaver Dam Eye Study. Ophthalmology, 1992; 99 (6): 933–943.
2. American Academy of Ophthalmology. Retina and Vitreous. American Academy of Ophthalmology Basic and Clinical Science Course, 2010-2011; 60-89.

3. **R. Klein, C F Chou.** Prevalence of Age-Related Macular Degeneration in the US Population. Arch Ophthalmol. 2011; 129 (1): 75-80.

4. Age-Related Eye Disease Study Research Group. 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 number 3 Ophthalmology, 2000; 107: 2224–32.

5. Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene and zinc for age-related macular degeneration and vision loss: AREDS report number 8. Arch Ophthalmol. 2001; 119: 1417-1436.

6. **Bakri SJ.** Macular Degeneration. Mayo Clinic Guide to Better Vision, 2007; 21-50.

7. **Votruba M, Gregor Z.** Neovascular age-related macular degeneration: present and future options. Eye, 2001; 15 (3): 424–29.

8. **Reeves BC, Harper RA, Russell WB.** Enhanced low vision rehabilitation for people with age related macular degeneration: a randomised controlled trial. Br J Ophthalmol. 2004; 88 (11): 1443–9.

9. **Snodderly DM.** Evidence for protection against age-related macular degeneration by carotenoids and antioxidant vitamins. Am J Clin Nutr. 1995; 1448-1461.

10. The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group, The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. N Engl J Med. 1994; 1029-1035.

11. **Friedman DS, O'Colmain BJ, Munoz B.** Prevalence of age – related macular degeneration in the United States. Arch Ophthalmol. 2004; 122: 564-72.

12. **T Krishnan, R D Ravindran.** Prevalence of Early and Late Age-Related Macular Degeneration in India: The INDEYE Study. Invest Ophthalmol Vis Sci. 2010 Feb; 51 (2): 701–707.

13. **Friedman DSKatz Jbressler NMRahmani Btielsch JM. R**acial differences in the prevalence of age-related macular degeneration: The Baltimore Eye Survey Ophthalmology, 1999; 106 (6) 1049-1055.

14. **Naghza, N Karam.** Epidemiology of Age Related Macular Degeneration (AMD) and It's Associated Ocular Conditions and Concomitant Systemic Diseases.Pak J Ophthalmol. 2013, Vol. 29 . 132-35.

15. **Wong TY, Loon S-C, Saw SM.** The epidemiology of age related eye diseases in Asia. British J Ophthalmol. 2006; 50-56.

16. **Thornton J, Edwards R, Mitchell P, et al.** Smoking and age-related macular degeneration: a review of association. Eye (Lond), 2005; 19: 935–44.

17. **Coleman HR, Chan CC, Ferris FL, 3rd, Chew EY.** Age-related macular degeneration. Lancet. 2008; 372: 1835–45.

18. **Arnarsson A, Sverrisson T, Stefánsson E, Sigurdsson H, Sasaki H, Sasaki K, et al.** Risk factors for five-year incident age-related macular degeneration: The Reykjavik Eye Study. Am J Ophthalmol. 2006; 142: 419–28.

19. **Ferris FL Davis MD Clemons TE et al.** The Age-Related Eye Disease Study Research Group, A simplified severity scale for age-related macular degeneration: AREDS Report No. 18. Arch Ophthalmol. 2005; 123 (11): 1570-1574.

20. **Zhou J, Pham L, Zhang N, He S, Gamulescu MA, Spee C, Ryan SJ, Hinton DR.** Neutrophils promote experimental choroidal neovascularization. Molecular vision, 2005; 11: 414–424.

21. **Popescu ML, Boisjoly H, Schmaltz H, Kergoat MJ, Rousseau J, Moghadaszadeh S, Djafari F, Freeman EE.** Explaining the relationship between three eye diseases and depressive symptoms in older adults. Invest Ophthalmol Vis Sci. 2012: 2308-13.

22. **Tatar O, Yoeruek E, Szurman P, Bartz-Schmidt KU, Adam A, Shinoda K, Eckardt C, Boeyden V, Claes C, Pertile G, et al.** Effect of bevacizumab on inflammation and proliferation in human choroidal neovascularization. Archives of ophthalmology, 2008; 126: 782–790.

23. **Davis MD Gangnon RE Lee LY et al.** The Age-Related Eye Disease Study Research Group, The Age-Related Eye Disease Study Severity Scale for age-related macular degeneration: AREDS Report No. 17. Arch Ophthalmol. 2005; 123 (11) 1484-1498 [erratum published in Arch Ophthalmol. 2006; 124 (2): 289-290].

24. **Chong EW, Simpson JA, Robman LD, Hodge AM, Aung KZ, English DR, et al.** Red meat and chicken consumption and its association with age-related macular degeneration. Am J Epidemiol. 2009; 169: 867–76.

25. **Montero JA, Ruiz – Moreno JM, Sanchis – Merino E, Perez– Martin S:** Systemic beta-blockers may reduce the need for repeated intravitreal injections in patients with wet age – related macular degeneration treated by bevacizumab. Retina. 2012; 24.

26. Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. Arch Ophthalmol. 2001; 119 (10): 1417–1436.

27. Age-Related Eye Disease Study 2 Research Group. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. JAMA. 2013; 309: 2005–2015.