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Original Research Article

Prevalence, Risk Factors, and Clinical Correlates of Age-Related Macular Degeneration in a Tertiary Care Setting of Western India

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Conflict of interest: Nil

Abstract:

Introduction: Age-related macular degeneration (AMD), a degenerative disorder of the macula causing irreversible central vision loss, significantly impacts quality of life. Its prevalence ranges from 1.4% to 3.1%. It is classified into dry (more common) and wet (less common but faster progressing) types, with pathogenesis involving complex interactions of environmental, genetic, and personal factors.

Aim & Objective: To estimate the prevalence and identify risk factors of AMD in a hospital-based population in Gujarat, India.

Materials & Methods: A cross-sectional study was conducted in the Department of Ophthalmology at a tertiary hospital over period of 2 years. Patients over 40 years old with drusen measuring 63 microns or more were included, while those with other retinal conditions or who did not consent were excluded. The study involved comprehensive eye examinations, fundus photography, and detailed patient histories.

Results: Prevalence of AMD was 2.15%. Early AMD was more prevalent (1.47%) than late AMD (0.67%), and dry AMD was more common (1.61%) than wet AMD (0.54%). Higher prevalence was observed in older age groups, smokers, alcohol consumers, obese individuals, those with hypertension, coronary artery disease, and a family history of AMD. Vision impairment and specific types of cataracts (nuclear and cortical) were also associated with higher AMD prevalence. No significant associations were found with gender, education, residence location, or diabetes.

Conclusion: The prevalence of AMD increases with age, obesity, hypertension, smoking, alcohol consumption, family history, vision impairment, and certain cataracts. Raising public awareness about AMD risk factors and promoting regular eye screenings, especially for older individuals and those with a family history, is recommended. Encouraging lifestyle changes like smoking cessation and moderating alcohol intake can also reduce AMD risk.

Keywords: Age-related macular degeneration (AMD), Family history, Obesity, Prevalence, Risk factors, Vision impairment,

Introduction

Age-related macular degeneration (AMD) is the leading cause of blindness in developed countries, especially among those older than 60 years, with an estimated 30-50 million people currently affected worldwide.[1] According to the World Health Organization (WHO), the number of individuals with AMD is projected to increase up to 288 million by 2040 if left uncontrolled and untreated. [2] Prevalence of AMD in India is 1.4–3.1%.[3,4] The economic burden of AMD treatment in India exceeds 1.5 billion USD annually, excluding indirect costs such as transportation, loss of income, and disability support. It is crucial to focus on early detection, surveillance of risk factors, and effective management strategies to mitigate the growing burden of AMD.[5]

AMD is a degenerative disorder primarily affecting the macula, leading to irreversible central visual loss. It begins with the buildup of lipoprotein deposits (drusen) and can significantly impact quality of life, resulting in decreased mobility, higher incidence of depression, loss of independence, and lower overall quality of life. [6]

The disease is conventionally classified into two types: dry (non-exudative, non-neovascular) and wet (exudative, neovascular). [7]

Dry AMD is more common and is characterized by significant atrophy of the outer retina and retinal pigmented epithelium (RPE), which can progress to geographic atrophy (GA). Treatment options for GA are limited. Wet AMD, although less common, progresses more rapidly to vision loss, with choroidal neovascularization (CNV) and pigment epithelial detachment (PED) being its main manifestations. This form is treated with intravitreal injections of anti-vascular endothelial growth factor (VEGF) inhibitors. In Asian populations, polypoidal choroidal vasculopathy (PCV) is a common variant of neovascular AMD. [8]

Early AMD is identified by drusen sizes between 63 microns and 125 microns without pigmentary abnormalities, while intermediate AMD features drusen larger than 125 microns with pigmentary changes. Late AMD includes neovascular AMD and/or geographic atrophy, with these changes occurring within two disc diameters of the fovea in either eye. The presence of intermediate drusen with pigmentary abnormalities has a low risk of progressing to late ARMD, but this risk increases significantly within five years. The presence of large drusen is associated with a 13% risk of progression to late ARMD.[7]

The pathogenesis of AMD involves a complex interaction of environmental, genetic, and personal factors. Aging leads to the accumulation of lipofuscin in retinal pigment epithelium (RPE) cells and dysfunction of the Bruch membrane, causing lipid and protein deposits. This results in the death of RPE and photoreceptor cells, leading to visual loss. Molecular factors like C-reactive protein (CRP) deposition in complement factor H individuals also contribute to AMD.[9] AMD is influenced by various systemic, genetic, and ocular risk factors. Key non-modifiable factors include age, female sex, white race, and genetics. Significant modifiable factors are smoking, hypertension, alcohol consumption, BMI, lifestyle, and sunlight exposure.[7] Few studies have been conducted in this region on the correlates of AMD. Therefore, we aim to estimate the prevalence, and identify risk factors of AMD in a hospital-based population.

Materials & Methods

This cross-sectional study was conducted in the Department of Ophthalmology at a tertiary hospital in Gujarat over period of 2 years. Patients over the age of 40 with drusen measuring 63 microns or more on fundoscopy were included in the study. Drusen size was determined by comparing it to half of the vein diameter at the optic disc margin, measured by a single vitreoretinal surgeon.

Exclusion criteria included patients with glaucoma, central serous retinopathy, diabetic retinopathy, hypertensive retinopathy, uveitis, anterior segment pathologies, small pupils, dense corneal and lens opacities impairing fundus examination, those with polypoidal choroidal vasculopathy, retinal angiomatous proliferation, myopic chorioretinal degeneration, or any macular dystrophies and those who did not provide valid consent.

A total of 2235 patients were attended to the ophthalmology department during study period, of whom 48 were diagnosed with AMD. Written informed consent was obtained from each subject. A general examination was conducted for all patients, documenting body mass index (BMI) and hypertension, and blood lipid levels were assessed. A comprehensive history was taken from all participants regarding smoking, alcohol consumption, physical activity, hypertension, and diabetes using a pre-designed proforma.

The examination followed a standardized protocol that included measuring visual acuity for distance with a Snellen chart, near vision with a Jaeger chart, intraocular pressure with an autorefractometer (POTEC PRK-7000) and a computerized noncontact tonometer (NIDEK NT-510), and anterior segment evaluation using slit-lamp biomicroscopy. Pupil dilation was achieved using tropicamide (0.8%) and phenylephrine (5%). Lens opacity was graded by comparing each eye with the Lens Opacities Classification System (LOCS III) photographs. Fundus findings were noted using direct and indirect ophthalmoscopy with a 20D lens and slit-lamp biomicroscopy with a 90D lens. Findings were classified according to an international classification and grading system for AMD. The features examined included hard and soft drusen, changes in the retinal pigment epithelium (RPE), geographic atrophy, choroidal neovascular membrane, and disciform scar.[10] AMD was classified as late (neovascular or geographic atrophy) or early (soft drusen or retinal RPE abnormalities). When both eyes of participants had lesions of different severity, the grade assigned was that of the more severely involved eye. Retinal lesions due to high myopia and inflammation were excluded. Retinal photographs were taken for documentation.

The data were analyzed using Microsoft Excel version 2015. Descriptive statistics were used to determine means and percentages. Variables were first tested for associations with AMD in a bivariate analysis using the Fisher exact test or chi-squared test, as appropriate. Variables associated with AMD ($p < 0.25$) in the bivariate analysis were further tested in a backward, stepwise multivariable logistic regression model adjusting for potential confounders and interactions. Odds ratios (OR) were calculated for the multivariable logistic regression. Statistical analysis was performed using SPSS version 12.0 for

Windows (SPSS, Chicago, IL). A two-tailed p-value < 0.05 was considered statistically significant.

Results

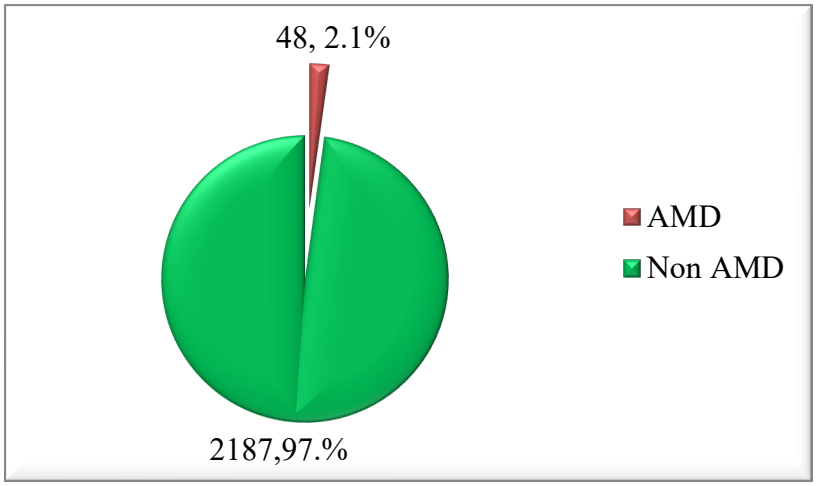

Figure 1: Prevalence of AMD

A total of 2235 patients were attended to the ophthalmology department during study period, of whom 48 were diagnosed with AMD. The prevalence of AMD was 2.15%.

Table 1: Type of AMD

Type of AMD	No of patients	Percentage out of 48 AMD patients (%)	Prevalence out of 2235 (%)
Early AMD	33	68.8	1.48
Late AMD	15	31.3	0.67
Dry AMD	36	75.0	1.61
Wet AMD	12	25.0	0.54

Early AMD affected 33 patients (68.8%), while Late AMD affected 15 patients (31.3%). Prevalence of early AMD was higher (1.47%) than late AMD (0.67%). Similarly, Dry AMD affected 36 patients (75.0%), compared to Wet AMD, which affected 12 patients (25.0%). Prevalence of Dry AMD was higher (1.61%) than wet AMD (0.54%) (Table 1).

Table 2: Age-Related Macular Degeneration (AMD) across various demographic and lifestyle factors

Characteristics	AMD (n-48)	Non AMD (n-2187)	Total (n-2235)	p value
Age group (years)				
41 to 50	7 (1%)	708 (99%)	715 (100%)	< 0.001
51 to 60	9 (1.3%)	663 (98.7%)	672 (100%)	
61 to 70	19 (3.7%)	499 (96.3%)	518 (100%)	
> 70	13 (3.9%)	97 (96.1%)	110 (100%)	
Gender				
Male	15 (1.6%)	901 (98.4%)	916 (100%)	0.16
Female	33 (2.5%)	1066 (97.5%)	1099 (100%)	
Education				
Illiterate	21 (2.6%)	801 (97.4%)	822 (100%)	0.31
Literate	27 (1.9%)	1166 (98.1%)	1193 (100%)	
Place of residence				
Urban	15 (2.1%)	711 (97.9%)	726 (100%)	0.85
Rural	33 (2.2%)	1256 (97.8%)	1289 (100%)	
Smoker				
Yes	22 (3.3%)	428 (96.7%)	450 (100%)	
No	26 (1.7%)	1539 (98.3%)	1565 (100%)	0.01
Alcoholic				
Yes	10 (3.9%)	245 (96.1%)	255 (100%)	
No	38 (1.9%)	1942 (98.1%)	1980 (100%)	0.03

Higher AMD prevalence in older age groups ($p < 0.001$), with 1% for 41-50 years, 1.3% for 51-60 years, 3.7% for 61-70 years, and 3.9% for those over 70. Smoking was associated with a higher prevalence of AMD at 3.3%, compared to 1.7% in non-smokers ($p = 0.01$). Alcohol consumption showed a 3.9% prevalence of AMD versus 1.9% for non-alcoholics ($p = 0.03$). Gender, education, and residence location were not significantly associated with AMD prevalence (Table 2).

Table 3: Association between AMD and comorbidities

BMI	AMD (n-48)	Non AMD (n-2187)	Total (n-2235)	p value
Normal	14 (1.8%)	744 (98.2%)	760 (100%)	0.01
Underweight	19 (1.9%)	979 (98.1%)	124	
Overweight	7 (2%)	338 (98%)	345 (100%)	
Obese	8 (6.1%)	124 (93.9%)	132 (100%)	
Hypertension				
Yes	23 (3.3%)	669 (96.7%)	692 (100%)	0.01
No	25 (1.6%)	1518 (98.4%)	1543 (100%)	
Diabetes				
Yes	12 (2.3%)	500 (97.7%)	512 (100%)	
No	36 (2.1%)	1687 (97.9%)	1723 (100%)	0.72
CAD				
No	22 (1.2%)	1760 (98.8%)	1782 (100)	< 0.001
Yes	26 (5.7%)	427 (94.2%)	427 (100)	

Regarding BMI, normal, underweight, and overweight individuals had AMD prevalence of 1.8%, 1.9%, and 2%, respectively, while obese individuals had higher prevalence (6.1%, $p = 0.01$). Patients with hypertension showed a 3.3% prevalence of AMD, compared to 1.6% patients without hypertension ($p = 0.01$). Patients with CAD had higher prevalence of AMD (5.7%) compared to patients without CAD ($p < 0.001$). Diabetes was not significantly associated with AMD prevalence (Table 3).

A family history of AMD was significantly associated with higher prevalence, with 8.5% of individuals with a family history having AMD compared to 1.4% without ($p < 0.001$). Vision impairment also showed a strong association, with 0.9% of those with normal vision, 5.2% of those with moderate visual impairment, and 5% of the blind having AMD ($p < 0.001$). Similarly, 4.1% of individuals with nuclear cataract had AMD compared to 1.3% without ($p < 0.001$). Cortical cataract was linked to a higher prevalence, with 6% of affected individuals having AMD versus 1.7% without ($p < 0.001$). However, posterior subcapsular cataract (3.3% vs. 1.9%, $p = 0.1$) and prior cataract surgery (3.9% vs. 2%, $p = 0.08$) were not significantly associated with AMD (Table 4).

Table 4: Prevalence of AMD in Relation to other factors

Family history of AMD	AMD (n-48)	Non AMD (n-2187)	Total (n-2235)	p value
Yes	19 (8.5%)	204 (91.5%)	223 (100%)	< 0.001
No	29 (1.4%)	1983 (98.6%)	2012 (100%)	
Vision impairment				
Normal	15 (0.9%)	1583 (99.1%)	1598 (100%)	< 0.001
MVI	25 (5.2%)	453 (94.8%)	478 (100%)	
Blind	8 (5%)	151 (95%)	159 (100%)	
Nuclear cataract				
Yes	28 (4.1%)	655 (95.9%)	683 (100%)	< 0.001
No	20 (1.3%)	1532 (98.7%)	1552 (100%)	
Cortical cataract				
Yes	14 (6%)	220 (94%)	234 (100%)	< 0.001
No	34 (1.7%)	1967 (98.3%)	2001 (100%)	
Posterior subcapsular cataract				
Yes	12 (3.3%)	357 (96.7%)	369 (100%)	0.1
No	36 (1.9%)	1830 (98.1%)	1866 (100%)	
Prior cataract surgery				
Yes	7 (3.9%)	172 (96.1%)	179 (100%)	0.08
No	41 (2%)	2015 (98%)	2056 (100%)	

Discussion

Prevalence of AMD: Age-related macular degeneration (AMD) is a significant public health concern globally, particularly due to its impact on vision among older adults. The prevalence of AMD varies widely across different populations and geographic regions, as evidenced by various studies. In our study, the prevalence of AMD was 2.15%, which aligns with findings from several other studies. The Andhra Pradesh Eye Disease Study and the Blue Mountain Eye Study reported AMD prevalence of 1.8%. [11] Lower prevalence rates were reported in other studies, including those by Hamati et al. [6] (1.68%), Kulkarni et al. [3] (1.38%), and Jayshree MP et al. [10] (0.46%). Sharma et al. [12] documented substantial regional variability, ranging from 1.8% in Karnataka to as high as 47.8% in central Maharashtra. These variations in prevalence rates may stem from differences in study design (community-based vs. hospital-based), methodological approaches, genetic predispositions, and environmental factors.

In our study, the prevalence of early AMD was higher (1.47%) than late AMD (0.67%). This distribution is consistent with findings from comparable studies. For example, the Aravind Comprehensive Eye Study reported a prevalence of 2.7% for early AMD and 0.6% for late AMD. [13] Similarly, the INDEYE population study documented rates of 2% for early AMD and 1.6% for late AMD. [14] Kulkarni et al. [3] found prevalence of 1.34% for early AMD and 0.37% for late AMD, which closely align with our results. While, Gupta et al. [15] reported higher rates of 4.7% for early AMD and 1.4% for late AMD. The predominance of early AMD observed in our study mirrors trends observed in the aforementioned studies, suggesting a common pattern across diverse populations.

Association of AMD with socio demographic characteristics: Our study identified a higher prevalence of AMD in older age groups, with a prevalence of 3.9% among individuals over 70 years of age. However, gender, education, and residence location were not significantly associated with AMD prevalence in our cohort. These findings are in alignment with other studies, though there are some notable differences. Hamati et al.[6] found that the prevalence was highest among those over 80 years, with the odds being 3.5 times greater than in the 60 to 70 year age group, indicating a significant risk increase in the oldest age groups. Mehta et al. [7] reported a striking increase in AMD prevalence from 7.69% in the 45-55 age group to 37.69% in the 66-75 age group. Age is the most consistent risk factor for AMD, with prevalence clearly increasing with advancing age. This highlights the need for targeted screening and preventive measures in older populations.

Gender differences in AMD prevalence have been reported inconsistently across studies. Hamati et al. [6] found that men have 16% higher odds of developing AMD than women. Conversely, Mehta et al. [7], along with several other studies, including Kulkarni et al. [3], Pokharel et al. [16], and Arnarsson et al. [17] suggest that AMD is more prevalent in females. The Age-Related Eye Disease Study (AREDS) reported that females were doubly affected by AMD compared to males. This disparity could be due to differences in study populations, genetic factors, or health behaviors that vary by gender.

The influence of residence location on AMD prevalence also varies. Hamati et al.[6] observed that individuals living in urban and metropolitan areas had higher odds of having AMD compared to those in rural areas. This urban-rural difference could be attributed to environmental factors, lifestyle differences, or access to healthcare services.

Smoking and alcohol as risk factor of AMD: Our study found higher prevalence rates of AMD among smokers (3.3%) and alcohol consumers (3.9%). These findings align with existing research indicating that smoking and alcohol consumption are significant risk factors for AMD.

Cigarette smoking is a well-documented risk factor for AMD. The Beaver Dam Eye Study (BDES) found that current smokers had a higher risk of developing large drusen and early AMD compared to former or never smokers. [18] The Age-Related Eye Disease Study (AREDS) also reported higher prevalence of large drusen, geographic atrophy, and neovascular AMD in smokers. [19] The Blue Mountains Eye Study (BMES) noted an increased 10-year incidence of AMD in both current and past smokers. [20] Mehta K's study showed that smokers have a 4.25 times higher risk of AMD progression compared to non-smokers. [7] Sharma et al. [12], and Velilla et al. [21] found strong correlations, with Velilla et al. [21] reporting a 6.6 times higher risk for smokers. Proposed mechanisms for this increased risk include adverse effects on blood lipids, increased oxidative stress, and reduced antioxidant levels.

Alcohol consumption has also been associated with higher AMD risk. Our study findings consistent with Sharma et al. [12] and Krishnaiah et al. [11], observed that alcohol drinkers were at a significantly higher risk of developing AMD compared to non-drinkers. The Los Angeles Latino Eye Study also found positive associations between alcohol consumption and AMD. [22]

Comorbidities as risk factor of AMD: Our study identified various comorbidities such as obesity, hypertension, CAD as significant risk factors for AMD. Our study found higher AMD prevalence among patients with hypertension (3.3%). Mehta K

et al.[7] and Sharma et al. [12] also found that diastolic blood pressure above 80 mmHg significantly increases the risk of AMD, with Mehta K noting a 2.5-fold higher risk. Untreated elevated blood pressure can exacerbate this risk over time.

Our study found a 6.1% AMD prevalence among obese individuals, supported by Seddon et al. [23], who found a correlation between higher BMI and AMD. Obesity may contribute to AMD through mechanisms such as systemic inflammation and oxidative stress. Knudtson et al. [24] demonstrated that an active lifestyle reduces AMD risk independently of other factors like BMI, smoking, and alcohol consumption. This suggests that promoting physical activity could be a valuable strategy in AMD prevention, particularly as individuals age.

Our study reported a 5.7% AMD prevalence in patients with CAD. The Singapore Indian Eye Study and BDES also linked cardiovascular risk factors, including CAD, to higher AMD odds, indicating that systemic vascular health is crucial in AMD development. [25] The Barbados Eye Study found a borderline significant link between diabetes mellitus and late AMD, highlighting the importance of managing systemic health to mitigate AMD risk. [26]

Association between Cataract and AMD: Our study found that nuclear cataract (4.1%) and cortical cataract (6%) are associated with a higher prevalence of AMD. posterior subcapsular cataract (3.3% vs. 1.9%, p = 0.1) and prior cataract surgery (3.9% vs. 2%, p = 0.08) were not significantly linked to AMD.

Supporting these findings, Hamati et al.[6] noted that cataract surgery slightly increased the odds of AMD (OR = 1.20), with 60% of AMD cases diagnosed within three months post-surgery, likely due to improved retinal visualization. Krishnaiah S et al.[3] reported that 9.86% of subjects with bilateral AMD had undergone bilateral cataract surgery, and 19.7% had undergone unilateral cataract surgery. Mixed cataracts (nuclear, cortical, and posterior subcapsular) were present in 26.76% of AMD patients. The APEDS study also found positive associations between cortical cataracts, cataract surgery, and AMD, suggesting an increased prevalence and long-term incidence of AMD post-surgery. These findings highlight the complex interplay between different types of cataracts, cataract surgery, and the development or diagnosis of AMD. Improved retinal visualization post-cataract surgery may explain the higher detection rates of pre-existing AMD, while the mixed cataract types in AMD patients indicate a potential common underlying pathophysiological mechanism.[11]

Conclusion

The study reveals that Early and dry AMD being more prevalent compared to late and wet AMD respectively. AMD prevalence increases notably with older age, obesity, hypertension, smoking, and alcohol consumption. Family history significantly increases the likelihood of developing the AMD. Vision impairment, nuclear and cortical cataracts are associated with higher AMD prevalence. Gender, education, residence location, and diabetes do not show significant associations.

Recommendation

It is recommended to raise public awareness about AMD risk factors and promote regular eye screenings, especially for older individuals and those with a family history of AMD. Lifestyle changes such as smoking cessation and moderation of alcohol intake should be encouraged to reduce AMD risk.

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