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Original Article

Prevalence of age-related macular degeneration and associated factors in Indian cohort in a tertiary care setting

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Purpose: To report a big data analysis of risk and protective factors in patients with AMD, as well as report on the age-adjusted prevalence in a geriatric Indian cohort in a hospital setting. **Methods:** This retrospective, observational study of all patients older than 60 years of age. Multiple logistic regression was performed for the binary outcome and the presence of AMD. Variables analyzed include age, gender, socioeconomic status, occupation, urban–rural–metropolitan distribution, self-reported history of diabetes mellitus (DM), hypertension (HTN), or coronary artery disease (CAD), ocular comorbidities, history of cataract surgery, and presenting VA. Odds ratios (OR) and 99% confidence intervals were calculated. **Results:** Of the 608,171 patients over the age of 60 years who attended our clinics, 1.68% of subjects had a diagnosis of AMD (N = 10,217). Less than half (4,621 of 10,217 with AMD) of them were diagnosed to have dry AMD. Cataract, glaucoma, and diabetic retinopathy were associated with lower risk of AMD. Cataract surgery was associated with the higher risk of AMD (OR = 1.20; 99% CI 1.13-1.29). Smoking was not associated with AMD. **Conclusion:** Big data analysis from a hospital setting shows that the prevalence of AMD above the age of 60 years is low. More patients with wet AMD present for treatment compared to dry AMD. Smoking was not associated with AMD in the Indian population. Cataract surgery was associated with higher prevalence of AMD.

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Age-related macular degeneration (AMD) is caused by a series of changes to the macula, typically beginning with build-up of lipoprotein deposits (drusen). The course of the disease varies among patients, but for many, it leads to irreversible central visual loss. This condition can be debilitating and has been associated with decreased mobility and falls, a higher incidence of depression, loss of independence, and lower overall quality of life.[1-3] AMD is estimated to affect 1.4–3.1% of people living in India, and its prevalence is expected to increase in the next several decades.[4,5] The economic burden of treatment of AMD in India is estimated to be more than 1.5 billion USD annually, and this does not include indirect costs such as transportation, loss of income, disability support, or the cost of complications from treatments.[6]

Dry AMD can be associated with significant atrophy of the outer retina and retinal pigmented epithelium (RPE) can lead to geographic atrophy (GA). Treatment options for GA are limited, though promising clinical trials are currently under way.[7] Alternatively, wet AMD can be caused by changes in the structure of choroidal, leading to choroidal neovascularization (CNV). The mainstay of treatment for wet AMD includes anti vascular endothelial growth factor (VEGF) inhibition by intravitreal injections. In Asian populations, polypoidal choroidal vasculopathy (PCV) is a common variant of neovascular AMD.[8,9]

Much effort has been directed toward identifying risk factors for AMD globally. Some of the more agreed upon nonmodifiable factors include increasing age, female sex, white race, and genetic factors.[10-12] Several modifiable risk factors have been assessed as well. Smoking and hypertension are well-studied modifiable risk factors for AMD.[13,14] More conservative associations between sunlight exposure, presence of cataracts, cataract surgery, BMI, and AMD have been identified.[15-17] The strength of these associations has varied greatly between studies and population. In this study, we perform a big data analysis of risk and protective factors in over 10,000 patients with AMD, as well as report on the age-adjusted prevalence in a geriatric Indian cohort in a hospital setting.

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Methods

This retrospective, observational study included all patients older than 60 years of age who presented to a large ophthalmology network in India from August 2010 to April 2020.

Patients filled out a standard consent form for electronic data privacy and use for research at the time of registration. Institutional review board approval was taken for the study (LEC-BHR-R-11-21-773). The study adhered to the Tenets of Declaration of Helsinki for human research.

The clinical data of each subject who underwent a comprehensive ophthalmic examination were entered into a browser-based electronic medical records system using a standardized template. The data points extracted for the study included demographic details, socioeconomic status (based on their ability to pay for the care), systemic illnesses, treatment outcomes, and ocular disease distribution. The systemic disease history was extracted using the Finite-state machine modelling algorithm.

In total, 10,217 patients above 60 years and older diagnosed with AMD in one or both eyes presented to the network during the study period and were included in this study.

Data were retrieved from the electronic record database and segregated in a single Excel sheet (Microsoft XL®). Data on patient demographics, clinical presentation, ocular diagnosis, and treatment modalities were used. Based on the diagnosis and clinical presentation, the patients were further classified into wet or dry AMD. Dry ARMD was diagnosed in eyes with intermediate or large drusen and had pigmentary abnormalities or geographic atrophy. Eyes with pigment epithelial detachment, choroidal neovascular membrane, or disciform scar with drusen in the same eye or fellow eye were diagnosed with wet ARMD. Standardized definitions were used for occupation, socioeconomic status, and geographic distribution. The visual acuity (VA) was classified according to the WHO guidelines.

Statistical analysis

Multiple logistic regression (MLR) was performed for the binary outcome and the presence of AMD. Variables analyzed include age, gender, socioeconomic status, occupation, urban–rural–metropolitan distribution, self-reported history of diabetes mellitus (DM), hypertension (HTN), or coronary artery disease (CAD), ocular comorbidities, history of cataract surgery, and presenting VA. Odds ratios (OR) and 99% confidence intervals were calculated using R software (version 3.5.1). A second regression model was run on a subset of the subjects for whom smoking status was available. Among subjects with AMD, MLRs were run for the presence of dry or wet AMD. For all models, an alpha level of 0.01 was assigned.

Results

Of the 608,171 patients over the age of 60 years who attended our clinics, 1.68% of subjects had a diagnosis of AMD (N = 10,217). Less than half (4,621 of 10,217 with AMD) of them were diagnosed to have dry AMD. Table 1 shows a baseline comparison of demographic and ocular risk factors between Individuals without AMD and AMD.

Table 1: Demographic and clinical profile of study population

	AMD (%) *n*=10217	No AMD (%) *n*=597954
Gender		
Female	4159 (41)	279316 (47)
Male	6058 (59)	318638 (53)
Age		
60-70 years	5541 (54)	443868 (74)
71-80 years	3592 (35)	131043 (22)
81-90 years	1015 (10)	21612 (4)
91-100 years	69 (1)	1431 (0)
Payer Status		
Paying	8015 (78)	362150 (61)
Nonpaying	2202 (22)	235804 (39)
Geography		
Metropolitan	1739 (17)	54953 (9)
Rural	3538 (35)	284001 (48)
Urban	4940 (48)	259000 (43)
Occupation		
Retired	2422 (24)	67955 (11)
Home Maker	2765 (27)	147669 (25)
Govt/Private Service	941 (9)	42498 (7)
Agriculture related	905 (9)	80672 (14)
Not Available/Not Applicable	2613 (26)	188203 (31)
Manual Labor	571 (5)	70957 (12)
Ocular Comorbidities		
Cataract	6658 (65)	460048 (77)
Glaucoma	460 (5)	37811 (6)
DR	243 (2)	24455 (4)
Cataract Surgery	4239 (41)	271414 (45)
Systemic Diseases		
Hypertension	2937 (29)	129557 (22)
Diabetes	2256 (22)	112378 (19)
Coronary Artery Disease	487 (5)	20891 (3)
Presenting Visual Acuity		
Mild or No Visual Impairment 0	1686 (16)	142399 (24)
Moderate Visual Impairment 1	3033 (30)	183127 (31)
Severe Visual Impairment 2	1251 (12)	39048 (6)
Blindness 3	3433 (34)	155253 (26)
Blindness 4	288 (3)	46895 (8)
Blindness 5	109 (1)	15830 (2)
Undetermined or Unspecified	417 (4)	15402 (3)

The overall prevalence of AMD was highest among the 60- to 69-year age group. However, the age-adjusted prevalence was highest above the age of 80 years, with the odds being 3.5 times compared to the 60- to 70-year age group. Among 10,217 patients with AMD, there were 4159 (41%) female and 6058 (59%) male patients.

In our cohort, 65% (n = 6679) people with AMD were from urban districts and metropolitan regions. A majority of patients (78%; n = 8015) paid for the services (upper socioeconomic class), and the overall prevalence of AMD

was significantly higher in this class of patients. The overall prevalence of AMD was high in home makers or individuals who had retired [Table 1].

Risk factors associated with the presence of AMD

In this dataset, we found that men have 16% higher odds of having AMD than women while controlling for the other factors [Table 2]. There was a statistically distinct difference in prevalence of AMD based on payer status, with paying patients having a higher prevalence (OR = 1.85). Individuals residing in urban and metropolitan areas had higher odds of having AMD than those residing in rural areas. Smoking status did not have any effect on the presence of AMD.

Subjects with cataract, glaucoma, and diabetic retinopathy (DR) were less likely to have AMD. Individuals with hypertension had higher odds of having AMD. Cataract surgery was associated with slightly higher odds of AMD (OR = 1.20). To further investigate the reason behind those undergoing cataract surgery having higher odds of AMD, a subanalysis was performed. The time duration between the cataract surgery and diagnosis of AMD was analyzed. It was observed that in 60% of individuals with AMD, it was diagnosed within 3 months of cataract surgery [Fig. 1]. This could be due to the better visualization of the retina after cataract surgery, and pre-existing AMD could be diagnosed after cataract surgery.

Table 3 shows demographic and clinical profiles of patients with wet and dry AMD. A subset analysis was performed to identify the risk factors of patients with wet AMD. The risk factors identified were the same as those observed in the cohort with AMD. In addition, individuals with HTN, DM, and CAD had higher risk of having wet AMD.

Discussion

Our study was hospital-based study of big data in AMD in the Indian population. In studies performed in Western countries, lower socioeconomic status (SES) has been associated with a higher prevalence of AMD.[18,19] In Asian populations, associations are less clear. The Andhra Pradesh Eye Study (APEDS) group similarly identified a potential association between lower SES and higher prevalence of AMD, although their findings were not statistically distinct.[15] The Singapore Malay Eye Study (SiMES) research team found no association between these two variables, although they identified an association between lower educational status and higher prevalence of AMD.[20] More recently, the Sankara Nethralaya Rural-Urban AMD (SN-RAM) study showed high prevalence of AMD in middle-class adults.[10] Our study, though hospital-based and should not be compared with population-based study, identified a higher prevalence of AMD in individuals with higher SES.

Table 2: Logistic regression analysis of factors associated with presence of AMD

	Odds Ratio	99% Confidence Interval		*P*
		Lower limit	Upper limit	
Age (Reference: 60-70 years)				
71-80 years	2.17	2.05	2.30	<0.001
81-90 years	3.51	3.19	3.85	<0.001
91-100 years	3.52	2.54	4.88	<0.001
Gender (Reference: Females)				
Male	1.16	1.07	1.25	<0.001
Payer Status (Reference: Nonpaying)				
Paying	1.85	1.72	1.99	<0.001
Geography (Reference: Rural)				
Metropolitan	1.77	1.63	1.92	<0.001
Urban	1.34	1.27	1.43	<0.001
Visual Acuity (Reference: Mild or No Visual Impairment 0)				
Moderate Visual Impairment 1	1.77	1.64	1.92	<0.001
Severe Visual Impairment 2	3.37	3.05	3.72	<0.001
Blindness 3	2.85	2.62	3.09	<0.001
Blindness 4	0.81	0.68	0.96	0.001
Blindness 5	0.66	0.51	0.85	<0.001
Ocular Comorbidities				
Cataract	0.45	0.42	0.49	<0.001
Glaucoma	0.55	0.48	0.62	<0.001
Diabetic retinopathy	0.39	0.33	0.47	<0.001
Cataract Surgery	1.20	1.13	1.29	<0.001
Systemic Diseases				
Hypertension	1.17	1.10	1.24	<0.001
Diabetes	0.99	0.92	1.06	0.710
Coronary Artery Disease	1.00	0.88	1.14	0.965

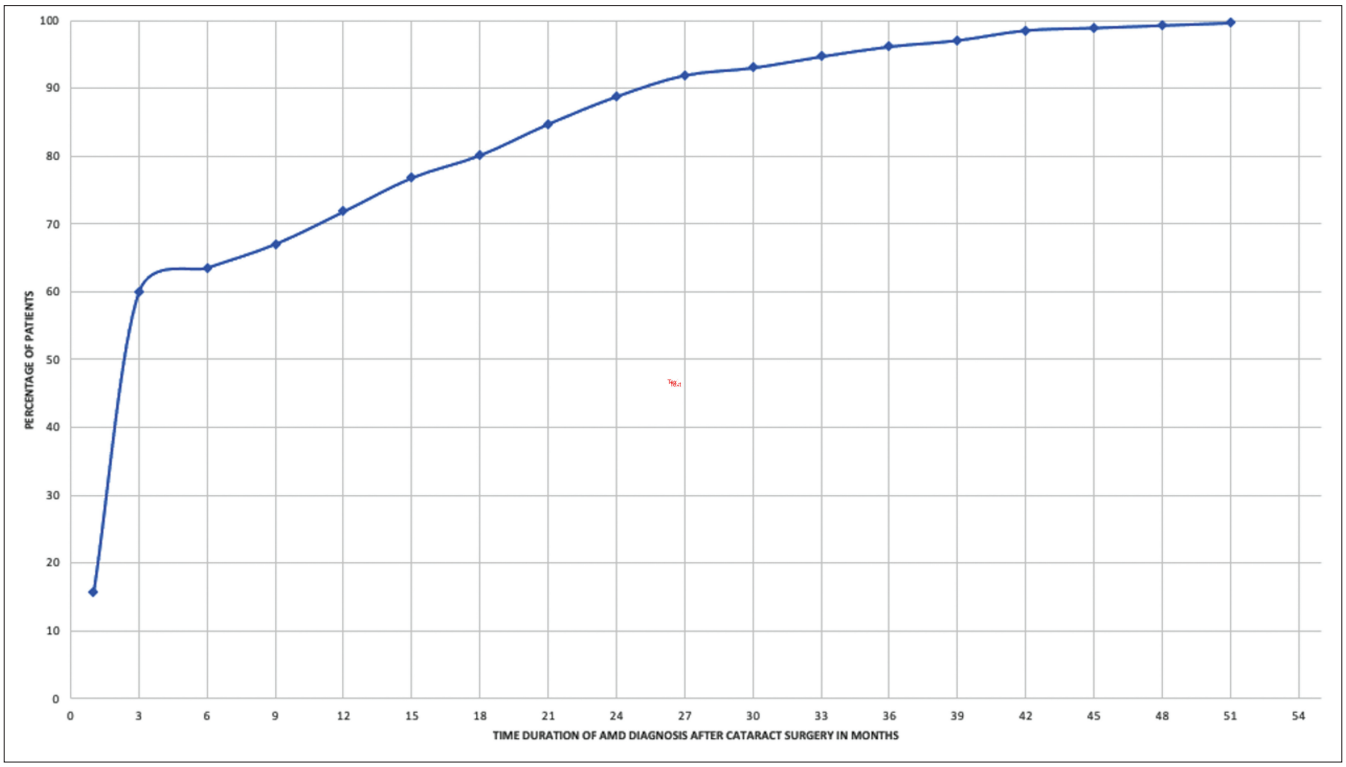

Figure 1: Percentage of patients versus time duration of AMD diagnosis after cataract surgery

There are a few key differences between each of these epidemiological studies. First, the comparable sample size in APEDS, SiMES, and SN-RAM was remarkably smaller than our sample size. Each study defined and operationalized SES differently. APEDS used primarily income strata. SiMES included education level, housing type, and income. SN-RAM utilized a questionnaire about patient assets (home ownership, possession of a television or vehicle). Our study used payer status (paying versus nonpaying). This may explain the variability in associations between SES and AMD.

There has also been controversy over the relationship between cataracts, cataract surgery, and prevalence of AMD. No association between cataracts and AMD was identified in multiple landmark studies, including the Beaver Dam Eye Study (BDES)[21] and the Blue Mountain Eye Study (BMES).[22] The Central India Eye and Medical Study reported similar results.[23] Positive associations between cortical cataracts, cataract surgery, and AMD were noted in the APEDS study.[15] Our study shows that cataracts are associated with lower prevalence of AMD, but this may represent underdiagnosis due to poor fundus visualization. This is supported by the drastic increase in AMD diagnoses within in the first 3 months after cataract surgery. Some evidence exists for increased prevalence and long-term incidence of AMD after cataract surgery.[15,21] Several hypotheses may explain this association, including a protective effect of the yellow-tinted natural lens against atmospheric blue light and postoperative inflammation exposing the macula to toxic substances.[24] Perhaps people may also have a genetic predisposition to the development of age-related ocular conditions that increase the odds of cataract development, surgical intervention, and AMD. It is possible that we identified a true association between cataract surgery and increased prevalence of AMD although our ratio is almost certainly inflated by under diagnosis of AMD prior to cataract extraction.

Many attempts at characterizing the relationship of systemic comorbidities and AMD have been made. The Barbados Eye Study group found a borderline-significant relationship between diabetes mellitus and late AMD.[25] The BDES found cardiovascular risk factors to be associated with AMD[26] and the Singapore Indian Eye Study group associated coronary artery disease with increased odds of AMD.[17] We also found higher odds of AMD in patients with DM and CAD. Provided that all three of these conditions involve unhealthy microvasculature, we are fairly confident that the associations we identified are true.

One of the best-studied risk factors for AMD is cigarette-smoking. The BDES was the first to report a strong association; current smokers had a higher risk of developing large drusen than former- or never-smokers and men who smoked cigarettes were more likely to develop early AMD.[27] The age-related eye disease study (AREDS) group found that smokers have a higher prevalence of large drusen, geographic atrophy, and neovascular AMD.[28] The BMES found an increased 10-year incidence of AMD in both current and past smokers.[14] In Indian populations, associations have been made between AMD and cigar smoking as well as smokeless tobacco.[10,15] We did not identify any statistically remarkable associations between smoking status and AMD in our study. It is probable that there is a confounder rather than a true lack of association between smoking and AMD, as this would go against most available research and our existing understanding of the association.

Table 3: Demographic and clinical profile of patients with dry and wet AMD

	Dry AMD (%) *n*=4621	Wet AMD (%) *n*=5596
Gender		
Female	2185 (47)	1974 (35)
Male	2436 (53)	3622 (65)
Age		
60-70 years	2733 (59)	2808 (50)
71-80 years	1492 (33)	2100 (38)
81-90 years	373 (8)	642 (11)
91-100 years	23 (0)	46 (1)
Payer Status		
Paying	3290 (71)	4725 (84)
Nonpaying	1331 (29)	871 (16)
Geography		
Metropolitan	697 (15)	1042 (18)
Rural	1656 (36)	1882 (34)
Urban	2268 (49)	2672 (48)
Ocular Comorbidities		
Cataract	3672 (79)	2986 (53)
Glaucoma	222 (5)	238 (4)
DR	119 (3)	124 (2)
Cataract Surgery	2251 (49)	1988 (36)
Systemic Diseases		
Hypertension	1231 (27)	1706 (30)
Diabetes	892 (19)	1364 (24)
Coronary Artery Disease	168 (4)	319 (6)
Presenting Visual Acuity		
Mild or No Visual Impairment 0	1245 (27)	441 (8)
Moderate Visual Impairment 1	1719 (37)	1314 (24)
Severe Visual Impairment 2	425 (9)	826 (15)
Blindness 3	900 (19)	2533 (45)
Blindness 4	163 (4)	125 (2)
Blindness 5	50 (1)	59 (1)
Undetermined or Unspecified	119 (3)	298 (5)

Our study has several limitations. The retrospective, cross-sectional nature of this study does not allow us to establish causality over associations. Our large sample size increases our chance of committing a type-one error. Lastly, the incomplete dataset on smoking prohibited us from controlling for smoking status in our regression analyses. For these reasons, we prioritized contextualizing our results with existing literature.

Our study is the first of this magnitude to evaluate the epidemiology of AMD in geriatric population in India in a tertiary care setting. Our large sample represents populations from all geographic regions of India, although our study population has less representation from adults over the age of 80 years. Our study can provide a benchmark for future hospital-based studies of AMD.

Conclusion

Big data analysis from a hospital setting shows that the prevalence of AMD above the age of 60 years is low. More patients with wet AMD present for treatment compared to dry AMD. Smoking was not associated with AMD in the Indian population.

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Conflicts of interest

There are no conflicts of interest.

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