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RESEARCH ARTICLE

PROGRESSION OF AGE RELATED MACULAR DEGENERATION AND DEVELOPMENT OF CHOROIDAL NEOVASCULARIZATION AND RISK FACTORS ASSOCIATED WITH IT IN PATIENTS OF AGE RELATED MACULAR DEGENERATION PRESENTING AT WEST ZONE REGIONAL INSTITUTE OF OPHTHALMOLOGY INDIA

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ABSTRACT

Purpose: Age related macular degeneration (AMD) is the leading cause of blindness in the developed world. Its incidence is on the rise in developing nations as well. Formation of choroidal neovascular membrane(CNVM) is the major cause of vision loss in AMD. Purpose of this study is to study the progression of AMD and risk factors associated with development of CNVM in Indian population. **Methods**: 200 eyes of 100 patients of more than 55 years of age presenting to our out patient department with AMD were selected and were followed for a period of 2 years. Progression of disease into active CNVM and conditions predisposing to its formation were analysed. **Results**: Progression of AMD into neovascular form (CNVM) is faster in the elderly population. Approximately 13% of patients developed CNVM within 1 year of presentation. Patients with large drusens, RPE abnormalities, serous PED have an increased risk of developing CNVM. Our study showed that, serous PED was the strongest risk factor in development of CNVM. **Conclusion**: Incidence of CNVM in AMD patients is more as compared to that of western population. Serous PED followed by a presence of both large drusens and RPE (Retinal Pigment Epithelium) abnormalities combined, are the major risk factors for Indian population. Early identification of risk factors and determining the major risk factors for development of CNVM in Indian population can help in early diagnosis and early treatment resulting in a better visual outcome.

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INTRODUCTION

Age related macular degeneration is the leading cause of irreversible blindness worldwide, accounting for 8.7% of cases of blindness globally [(1)].However in developing countries, it has been overshadowed by other more common causes of blindness like Cataract (62.6%), Refractive Errors (19.70%), Glaucoma (5.80%) etc.[(2)] Nevertheless, due to changing demographic patterns and a rising elderly population, ARMD is likely to have a greater impact in the years to come. Age related macular degeneration is a degenerative disorder affecting the macula.

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It is characterized by the presence of specific clinical findings, such as drusen, geographic atrophy, pigment epithelialdetachment (PED) and /or CNVM (Choroidal neovascular membrane) in a patient over the age of 50 years, in the absence of another disorder. [(3)] Manifestations of AMD can broadly be divided into two categories 1) Non-neovascular or Dry (atrophic) AMD (90%) and 2) Neovascular or Wet (exudative) AMD (10%). Dry AMD is far more common than the wet form. A small number of patients with dry AMD will proceed to the wet form. Wet form is characterized be the development of Choroidal Neovascular Membrane and is the major cause of vision loss in people with AMD.[(3)] Studies like MARINA and ANCHOR which study the result of anti-VEGF on wet AMD imply that early diagnosis and prompt treatment is essential for better visual outcome. Thus it is essential to study which eyes with dry ARMD are more likely to progress to the dreaded wet form.

There was 10 % cumulative incidence of CNVM for a period of 6.3 years in Age Related Eye Disease Study Group [6]. In various other studies like Macular Photocoagulation study, Beaver Dam eye study etc. It has been found to range from, 4 % to 20 %. Also, in these studies, various phenotypic risk factors related to development of CNVM like drusen size and retinal pigmentary abnormalities were studied. [7][8][9]All of these studies show the progression of AMD in western population. In our study, we aim to evaluate the progression of disease and predisposing factors of CNVM in Indian population.

MATERIALS AND METHODS

This Prospective Observational Study was done in M and J West Zone Regional Institute of Ophthalmology BJ Medical College, Ahmedabad, Gujarat. 200 eyes of 100 patients aged more than 55 years with AMD presenting to the out patient department were selected and observed for a period of 1 year after obtaining an informed written consent. The total study period extended from May 2017 to Jan 2019. Patients who had already developed CNVM in either of the eye and patients with other causes of maculopathy like angioid streaks, pathological myopia, central serous retinopathy and polypoidal choroidal vasculopathy were excluded. Also patients with high myopia, chronic uveitis, diabetic retinopathy, hypertensive retinopathy and mature catarat and patients who were unwilling or lost on follow up were excluded.

Vision in both eyes was tested using Snellen's visual acuity chart. Intraocular pressure was measured using Goldman's applanation tonometer. Dilated and undilatedanterior segment examinationswere performed by slit lamp biomocroscopy. Fundus examination was done using direct ophthalmoscope, indirect ophthalmoscope, 90D lens and Goldman 3 mirror lens after dilatation with 0.8% Tropicamide and 5% phenylephrine. Fundus photographs was taken (using Carl Zeiss Meditec AG). FFA was done with 5 ml of 10% sodium flouresceininjectedintravenously (usingCarl Zeiss Meditec AG). OCT was done (with TOPCON 3D OCT). Based on these findings at the beginning of the study, patients were divided into 5 mutually exclusive risk factor groups.

Group A	Large drusens without RPE abnormalities
Group B	RPE abnormalities without large drusens
Group C	Large drusens with RPE abnormalities
Group D	Serous PED
Group E	Small or intermediate sized drusens with or without RPE abnormalities

*small drusen (<63 µm), intermediate drusen (>63 µm but <125 µm), Large drusen (>125 µm)

**RPE abnormalities: any definite hyper- or hypopigmentaryabnormalities of retinal pigment epithelium associated with medium or large drusen but not due to other known disease.

***The size of drusen can be estimated by comparison with the approximately 125 µm diameter of a retinal vein at the optic disc margin.[3]

Patients were followed up on 3 monthly basis or as and when a new symptom appearedup to the period of 1 year. At each visit patients were assessed for BCVA, fundus examination,macular thickness (using OCT). FFA was done at presentation, at the end of 6 months, 1 year and as and when symptoms and signs of CNVM developed in the intervening period. Incidence of CNVM at end of 6 months and 1 year was calculated. Progression of disease into active CNVM and conditions predisposing to its formation were analysed. The results were analysed using, one sample t test and chi square test.

RESULTS

200 eyes of 100 patients with Age related Macular Degeneration (AMD) were studied and followed over a period of one year. Age distribution of the study population is shown below (Figure 1). Most of the patients of AMD were between ages of 75-85 years. The distribution of risk factors in the study population at baseline is also illustrated below(Figure 2), with more than half of the eyes having only lower grades of AMD. Out of, 200 eyes, 26 eyes of 23 patients developed Choroidal neovascular membrane (CNVM). 20 patients had unilateral disease whereas 3 patients developed CNVM in both eyes. Out of 26 eyes, 14 eyes developed CNVM in first 6 months whereas 12 eyes developed cnvm in the later 6 months. Mean age of study population was 69.9 ± 7.8 years whereas mean age of patients developing CNVM was found to be 71.2±6.5 years. Incidence of CNVM was found to be increasing with age.(5.8% between 55-64 years vs. 25% above 85 years of age) however this data was not found to be statistically significant($p = 0.11$). Age distribution data of the patients is mentioned below (Table 1) (Figure 3,4). Among various risk factor groups, maximum incidence of CNVM was found to be in patients with serous PED (Group D), with 3 out of 6 patients (50%) developing CNVM. This was found to be statistically significant ($p < 0.05$) with odds ratio of 7.43. This was closely followed by Group C i.e. patients with both large drusens and RPE abnormalities (40%).Risk of developing CNVM was found to be statistically significant in this group as well ($p < 0.05$) and an odds ratio of 6 Of patients with large drusens only without RPE abnormalities (Group A) 17.78 % and among patients with RPE abnormalities only (Group B), 12.50% developed CNVM. This relation however was not found to be statistically significant. Only 3.8% patients without aforementioned risk factors developed the disease. i.e. Group E. This was too found to be statistically significant ($p < 0.05$) with an odds ratio 0.131. (Figure 4,5).

DISCUSSION

Our study yields an incidence of development of CNVM in patients of ARMD, at 13% per year. This is considerably higher than the annual incidence of CNVM found in other studies; 10 % cumulative incidence for a period of 6.3 years found in Age Related Eye Disease Study Group[6]. In various other studies it has been found to range from, 4 % to 20 % [7][8][9]. This could be due to an actual difference between Indian and Western Population or due to sample variability or due to a small sample size. Also most of the studies calculate a cumulative incidence of CNVM over 5-10 years, whereas we have followed up the patients only for a period of 1 year. Our study shows an increased incidence of CNVM with an increase in age; incidence being 6.25% between 55-64 years of age vs. 33.33% over 85 years of age. However this was not found to be statistically significant (p=0.11). Various studies Indian as well as western world, show a very strong correlation between age and development of CNVM.[10][11][12] This lack of significance could be due to, a small sample size, with a follow-up period only 1 year. Another possible reason is that only 4 eyes of 2 patients, were above 85 years of age were included in the study. This could be explained by higher mortality in India of patients above 85 years of age.

Table 1.

Age wise incidence of CNVM				
Age	Total no of patients	CNVM in 1st 6 months	CNVM in next 6 months	Total incidence of CNVM
55-65 y	34	1	1	2
65-75y	58	3	4	7
75-85y	104	9	7	16
85-95y	4	1	0	1
Total	200	14	12	26

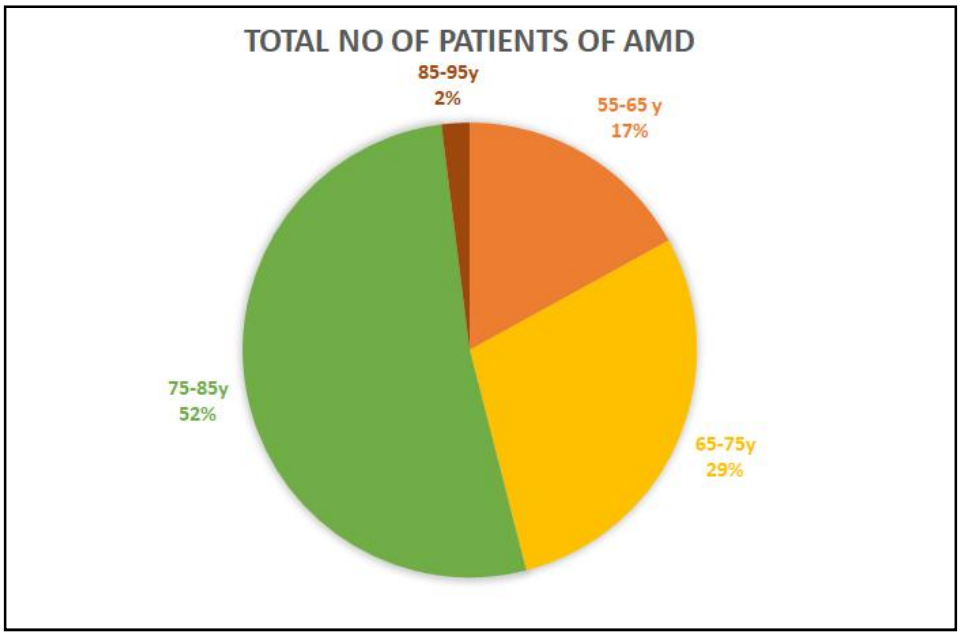
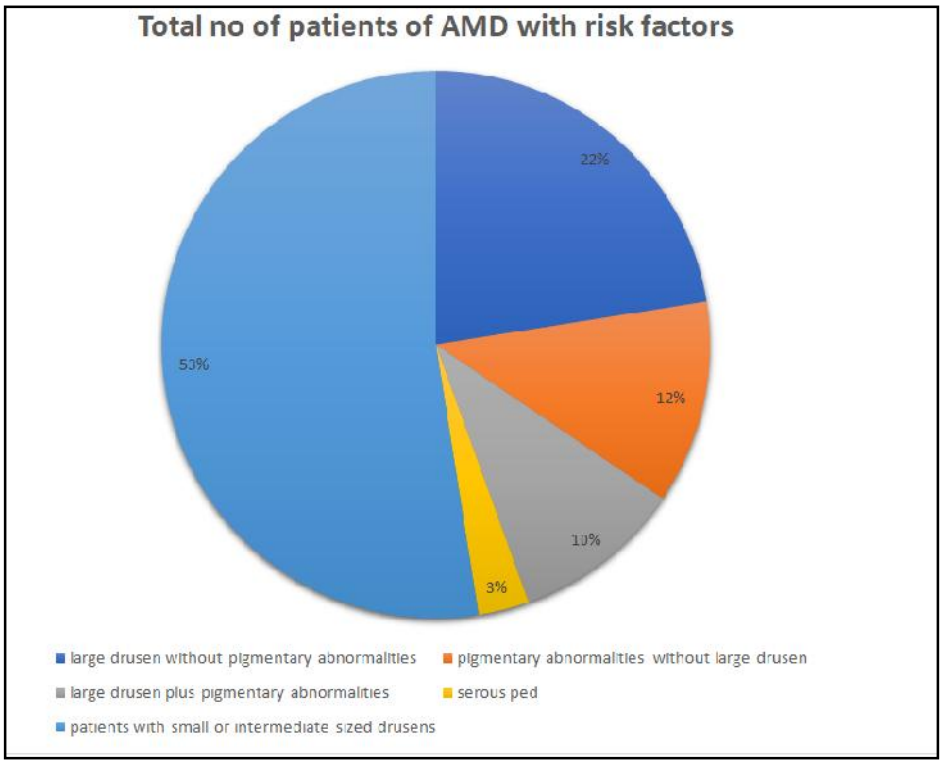


Figure 1.



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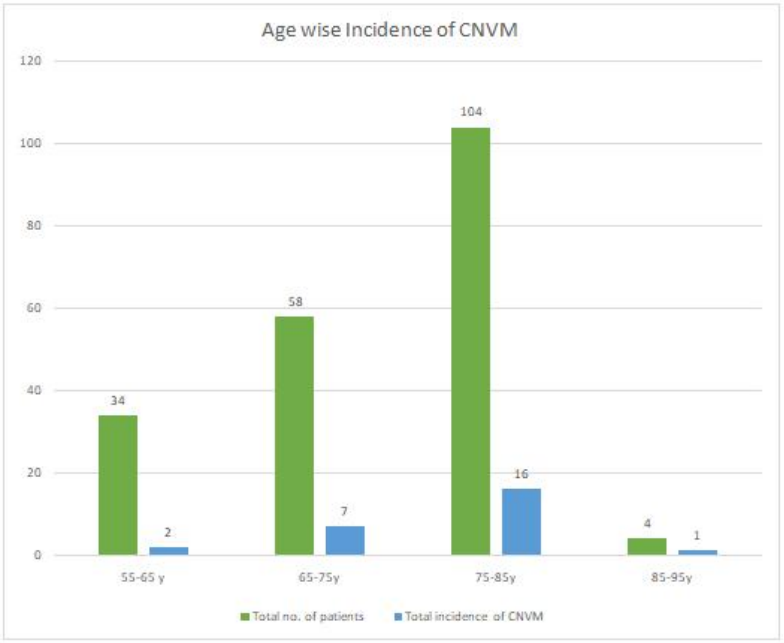

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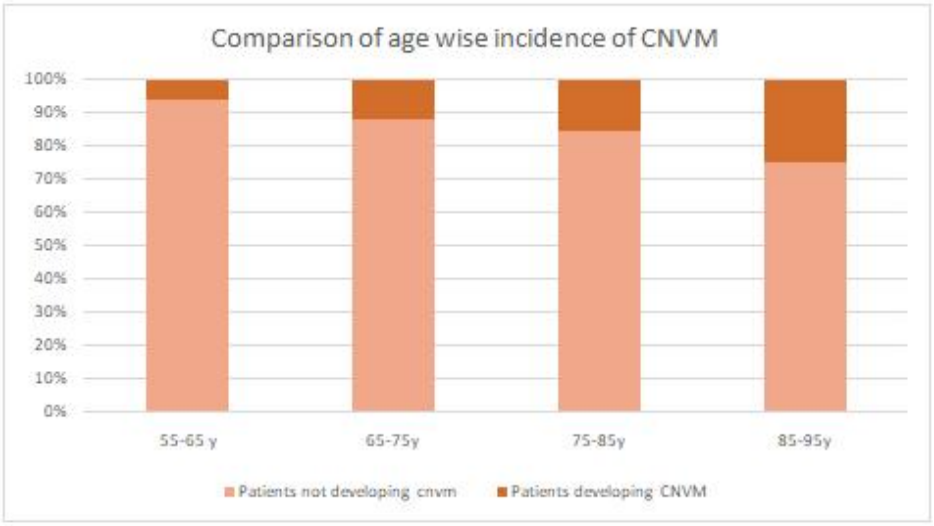

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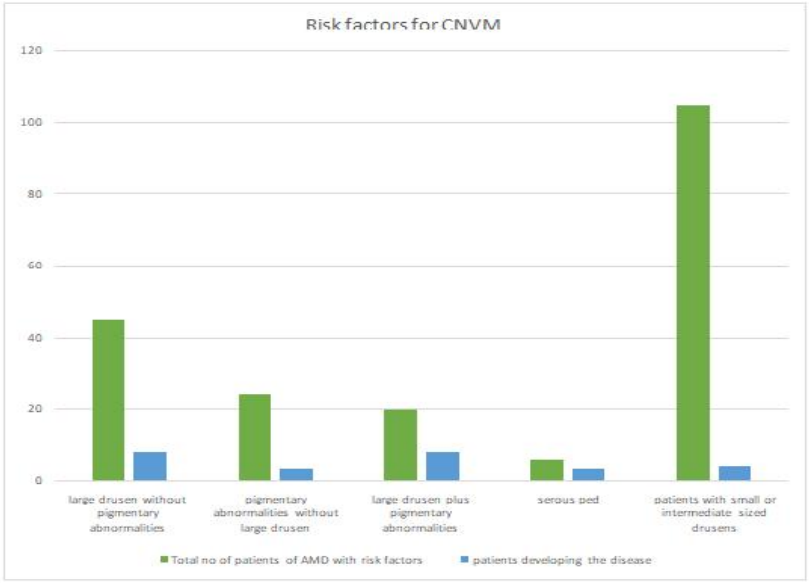

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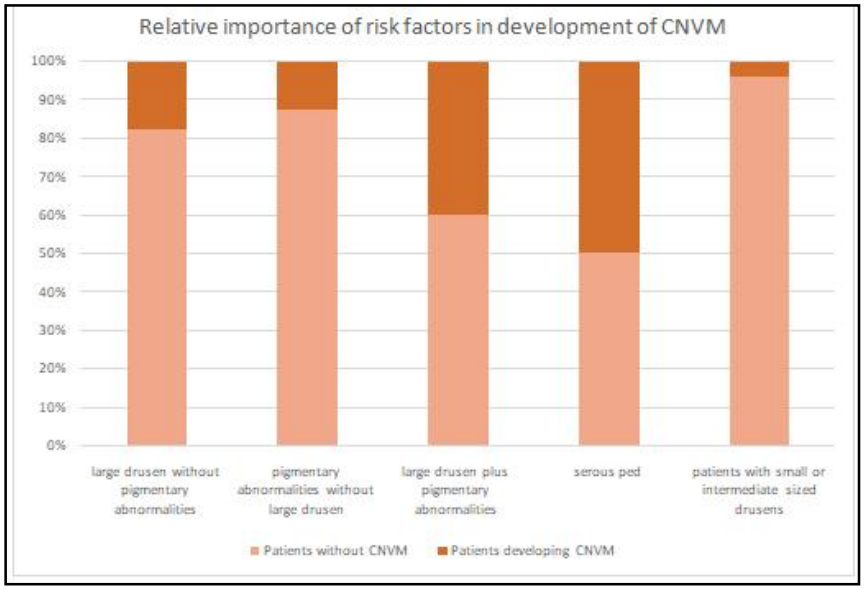

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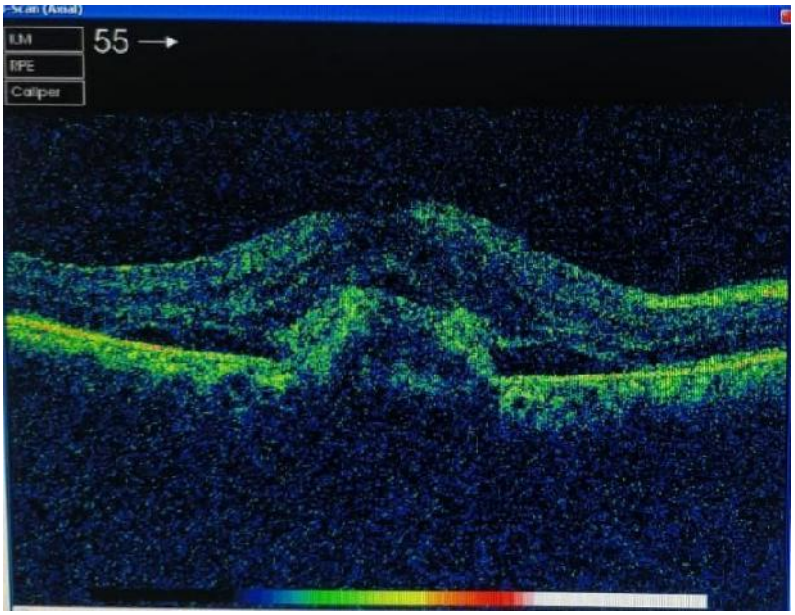

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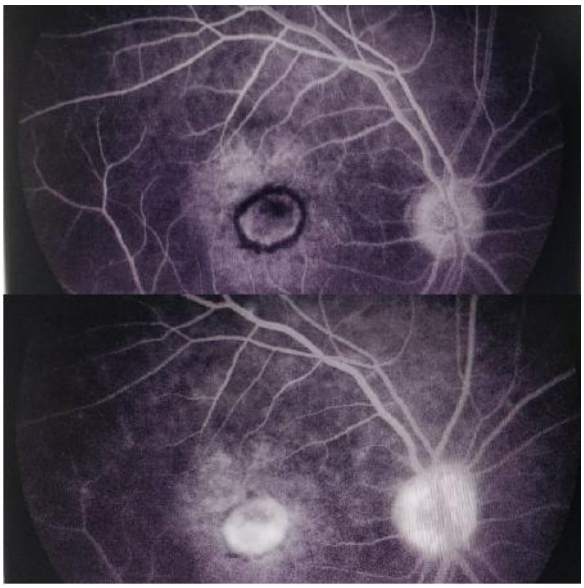

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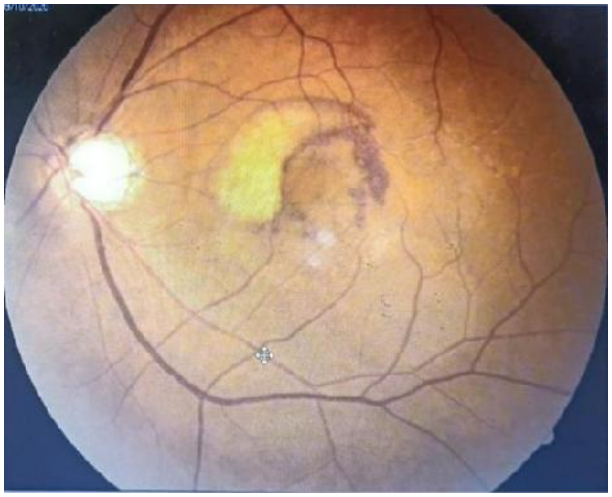

Figure 9.

In various studies development of CNVM in eyes with serous PED has been to be high, ranging from 28-32%.[14][15] Conversion rate in our study was found to be 50 %, with both the patients being above 75 years of age, with odds ratio 7.43 ($p<0.05$), making serous PED, the major risk factor. Macular Photocoagulation study group demonstrated that the presence of large drusen and focal hyper pigmentation of the retinal pigment epithelium were independent risk factors for development of neovascularization (relative risk, 2.4 and 2.5, respectively). Only 10% of eyes with no large drusen or any retinal pigment epithelial hyper pigmentation compared with 58% of eyes with both large drusen and retinal pigment epithelial hyper pigmentation developed neovascularization in the fellow eye within 5 years.[13] In our study, risk of developing CNVM was found to be 40% in patients with both large drusens and RPE abnormalities ($p<0.05$).Various other studies like Age Related Eye Disease Study, Blue Mountains Study, CAPT (Complications of Age-related Macular Degeneration Prevention Trial)Research group etc. too have found a strong correlation between development of CNVM and the presence of large drusens and pigmentary changes [14][15][16][17][18]

Conclusion

Incidence of CNVM in AMD patients in India is more as compared to that of western population. Increasing age is associated with an increase in risk of both ARMD and CNVM. Serous PED is the major predisposing risk factor correlated to development of CNVM. Presence of both large drusens and RPE abnormalities are far more likely to cause CNVM than either of them individually. Early identification of risk factors and determining the major risk factors for development of CNVM in Indian population can help in early diagnosis and early treatment resulting in a better visual outcome.

Conflicts of interest and Financial disclosure

The authors have no conflicts of interest to declare.
There is no financial interest to report.

GLOSSARY OF ABBREVIATIONS

AMD: Age Related Macular Degeneration
ARMD: Age Related Macular Degeneration
BCVA: Best Corrected Visual Acuity
CNVM: Choroidal Neovascular Membrane
FFA: Fundus Fluorescein Angiography
OCT: Optical Coherence Tomography
PED: Pigment Epithelium Detachment
RPE: Retinal Pigment Epithelium

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