

# Age-related macular degeneration in Singapore

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## ABSTRACT

**Introduction:** This study aimed to describe the morphology of age-related macular degeneration (AMD) as well as to obtain an estimate of the population-based incidence rate in Singapore.

**Methods:** This is a retrospective hospital-based study of AMD cases seen in 1991 and 1992 at the Singapore National Eye Centre (SNEC), a tertiary eye centre. All case notes recorded with the International Classification of Diseases, ninth revision, clinical modification code '362.5', which is 'degenerations of the macula', were retrieved and analysed. Only case notes of patients who were aged 50 years and above and with documented AMD were included in the study.

**Results:** There were 41 (21.8 percent) patients with drusen alone, 39 (20.7 percent) with dry AMD and 108 (57.5 percent) with exudative AMD. The morphology of the disease was similar among the Chinese and non-Chinese and there were no gender differences. A significant majority of patients with dry and exudative AMD had legal blindness at presentation (p-value is less than 0.0001). Notably, 27 (33.3 percent) patients with exudative AMD had improved vision with time. In comparison, the majority of patients with dry AMD or drusen alone tended to have the same or worsening visual acuity over time. The two-year SNEC hospital incidence rate of AMD in 1991–1992 was 0.38 percent or equivalent to 3.8 per 1,000 new cases seen at SNEC. The estimated population-based incidence rate of exudative AMD was 0.02 percent.

**Conclusion:** The population incidence of exudative AMD is lower but comparable to the Western population. Patients with exudative AMD tend to have poorer vision as compared to patients with geographical atrophy or drusen. The proportion of exudative AMD to geographical atrophy appears to be higher than in the West.

**Keywords:** age-related macular degeneration, drusen, dry age-related macular degeneration, exudative age-related macular degeneration, macular degeneration

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## INTRODUCTION

Age-related macular degeneration (AMD) is a degenerative disorder of the central area of the retina often associated with visual impairment, which is more frequent after 50 years of age.<sup>(1)</sup> It is registered in Europe and the United States as the commonest cause of blindness after age 60 years. It was previously thought to be a disease predominant in whites and rare in Asians. However, recently, Oshima et al had found the prevalence of exudative AMD in Japan to be 0.67%.<sup>(2)</sup> Yuzawa et al, in a nationwide survey in Japan, had also reported a 1.7-fold increase in the annual number of exudative AMD over six years (1987–1993).<sup>(3)</sup> These studies suggest that AMD is becoming an important cause of visual loss in Asians. The aim of this study is to describe the morphology of AMD as well as to obtain an estimate of the population-based incidence rate in Singapore.

## METHODS

This is a retrospective hospital-based analysis of the incidence and morphology of AMD seen in a tertiary hospital in 1991 and 1992. This national general eye hospital handles 150,000 outpatient attendances and 8,000 major eye operations per annum, equivalent to about 40% of the total attendance at all hospitals in Singapore. All case notes of patients with an International Classification of Diseases, ninth revision, clinical modification code 362.5, which is "degenerations of the macula", were retrieved and analysed. Only case notes of patients who were aged 50 years and older and with documented AMD were included in the study. A total of 114 patients were included in the study. The age, gender, best-corrected Snellen visual acuity at presentation and subsequent visits, the laterality of involvement, type of AMD lesion, duration of symptoms, fundus fluorescence angiographies, as well as any intervention were documented for each patient.

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**Table I. Characteristics of patients with different age-related macular degeneration morphology admitted to the Singapore National Eye Centre in 1991–2.**

Characteristics	No. (%) drusen alone (n = 15)	No. (%) global atrophy (n = 18)	No. (%) exudative AMD (n = 81)	p-value
Age (years)*	66.1 ± 9.2	66.5 ± 8.4	68.6 ± 8.0	0.17
Gender				
Male	4 (26.7)	11 (61.1)	46 (56.8)	0.088
Female	11 (73.3)	7 (38.9)	35 (43.2)	
Race				
Chinese	15 (100.0)	15 (83.3)	66 (84.2)	0.19
Non-Chinese	0 (0.0)	3 (16.6)	15 (15.8)	
Visual acuity at presentation				
≥ 6/9	9 (60.0)	2 (11.1)	7 (8.6)	< 0.0001
6/12	3 (20.0)	1 (5.6)	5 (6.2)	
6/18	1 (6.7)	2 (11.1)	6 (7.4)	
6/24	1 (6.7)	1 (5.6)	4 (4.9)	
6/36	1 (6.7)	1 (5.6)	8 (9.9)	
6/60	0 (0.0)	2 (11.1)	5 (6.2)	
6/120	0 (0.0)	2 (11.1)	6 (7.4)	
Counting fingers	0 (0.0)	6 (33.3)	35 (43.2)	
Hand movement	0 (0.0)	1 (5.6)	5 (6.2)	
Perception of light	0 (0.0)	0 (0.0)	0 (0.0)	
No light perception	0 (0.0)	0 (0.0)	0 (0.0)	
Legal blindness (worse than 6/60)				
Yes	0 (0.0)	11 (61.1)	51 (63.0)	< 0.0001
No	15 (100.0)	7 (38.9)	30 (37.0)	
Change in visual acuity				
Worse	6 (40.0)	4 (22.2)	8 (9.9)	0.65
No change	9 (60.0)	13 (72.2)	46 (56.8)	
Better	0 (0.0)	1 (5.6)	27 (33.3)	

\* expressed as mean ± standard deviation

AMD is defined based on the criteria described by the International ARM Epidemiological Study Group.<sup>(1)</sup> It is a disorder of the macular area of the retina, most often clinically apparent after 50 years of age, characterised by any of the following primary items, without indication that they are secondary to another disorder (e.g. ocular trauma, retinal detachment, high myopia, chorioretinal infective or inflammatory process, choroidal dystrophy):

- Drusen: discrete whitish-yellow spots, which are external to the neuroretinal or the retinal pigment epithelium (RPE).
- Dry AMD: any sharply-delineated roughly round or oval area of hypopigmentation or depigmentation.
- Exudative AMD: RPE detachments, subretinal or sub-RPE neovascular membranes, subretinal haemorrhages, epiretinal, intraretinal, subretinal or sub-RPE scar/glia tissue.

The cases were classified into the three main categories of drusen only, dry AMD and exudative AMD.

The data was recorded on an Excel® spreadsheet and analysed with the Statistical Package for Social Sciences version 7.5 (SPSS Inc, Chicago, IL, USA). The mathematical estimation of the population age-matched incidence of exudative AMD is as follows: the total number of cataract surgeries performed in Singapore

from January 1992 to December 1992 was 7,930.<sup>(4)</sup> The total number of cataract surgeries performed in this hospital during the same period was 3,174.<sup>(4)</sup> The relative proportion of cataract surgery performed in this hospital with respect to the total number performed in Singapore in 1992 was calculated to be 0.4. The number of patients with exudative AMD in this hospital in 1991–1992 was 81. The extrapolated number of exudative AMD seen in all hospitals in Singapore is therefore estimated to be 81/0.4, equivalent to 202.5. The population census estimation of the number of people aged 50 years and older residing in Singapore during this period was 489,100.<sup>(5)</sup> The two-year population-based incidence of exudative AMD in Singapore residents aged 50 years and older was calculated to be 202.5/489,100, which is 0.04%.

## RESULTS

A total of 248 patients were identified from which 237 case notes were retrieved and analysed, while 11 case notes were missing or destroyed. Another 123 case notes were miscoded for macular diseases other than AMD. These were diabetic maculopathy, myopic degeneration, macular holes and central serous retinopathy.

A total of 114 patients were included in the study.

**Table II. Morphology and progression of AMD in five patients.**

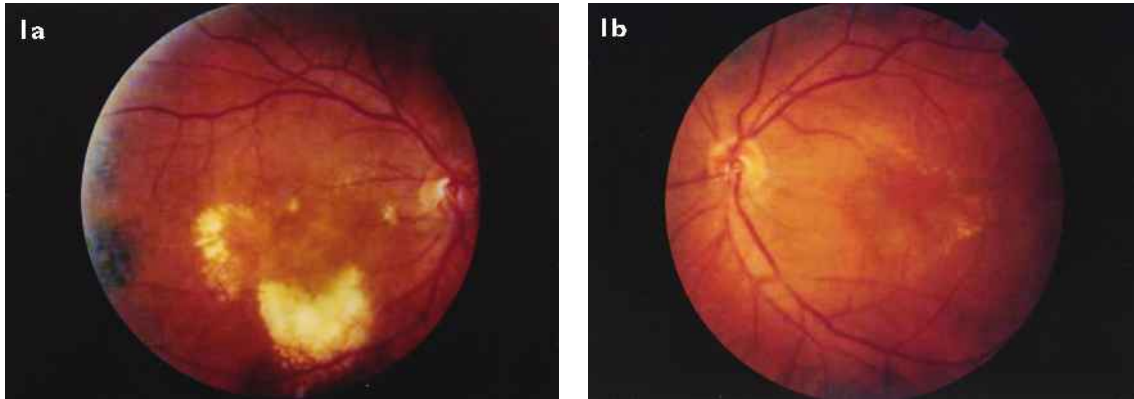
Presentation	Progression
Case 1 (Fig. 1) 66 years, Chinese male BCVA 6/120 OD 6/12 OS OD <ul style="list-style-type: none"> <li>Subretinal haemorrhage and exudates in posterior pole</li> </ul> OS <ul style="list-style-type: none"> <li>Extra-foveal CNV</li> </ul>	OD <ul style="list-style-type: none"> <li>Developed breakthrough vitreous hemorrhage at seventh year of follow-up.</li> </ul> OS <ul style="list-style-type: none"> <li>Treated with focal argon laser photocoagulation.</li> <li>Post-laser FFA showed obliteration of CNV.</li> <li>Developed occulted CNV 18 months post-laser. No treatment performed.</li> <li>BCVA maintained at 6/30 for the next seven years.</li> </ul>
Case 2 (Fig. 2) 67 years, Chinese female BCVA 6/18 OD 6/18 OS OU <ul style="list-style-type: none"> <li>Geographical atrophy</li> </ul>	OU <ul style="list-style-type: none"> <li>BCVA progressively decreased to 6/60 over five years of follow-up.</li> </ul>
Case 3 (Fig. 3) 69 years, Chinese male BCVA CF OD 6/24 OS OD <ul style="list-style-type: none"> <li>Disciform scar at macula</li> </ul> OS <ul style="list-style-type: none"> <li>Pigment epithelial detachment with subretinal haemorrhage and exudates</li> </ul>	OD <ul style="list-style-type: none"> <li>BCVA maintained at CF eighth year of follow-up.</li> </ul> OS <ul style="list-style-type: none"> <li>Treated with focal argon laser photocoagulation.</li> <li>Cataract extraction with posterior chamber IOL at fourth year of follow-up.</li> <li>BCVA progressively reduced to CF at eighth year of follow-up.</li> </ul>
Case 4 71 years, Chinese female BCVA 6/24 OD 6/15 OS OD <ul style="list-style-type: none"> <li>Extrafoveal Pigment epithelium detachment</li> </ul> OS <ul style="list-style-type: none"> <li>Subretinal haemorrhage and exudates at the macula</li> <li>Patient refused FFA and treatment.</li> </ul>	OD <ul style="list-style-type: none"> <li>BCVA maintained at 6/18 at eighth year of follow-up.</li> </ul> OS <ul style="list-style-type: none"> <li>Developed disciform macular scar with BCVA reduced to CF at eighth year of follow-up.</li> </ul>
Case 5 83 years, Chinese female BCVA 6/60 OD 6/18 OS OD <ul style="list-style-type: none"> <li>Breakthrough vitreous haemorrhage</li> </ul> OS <ul style="list-style-type: none"> <li>Confluent soft drusen at the macula</li> </ul>	OD <ul style="list-style-type: none"> <li>Developed disciform scarring with vision reduced to CF at eighth year of follow-up.</li> </ul> OS <ul style="list-style-type: none"> <li>BCVA remained stable at 6/18 at eighth year of follow-up with no evidence of CNV.</li> </ul>

BCVA: best corrected visual acuity; CNV: choroidal neovascularisation; FFA: fundus fluorescence angiogram; IOL: intraocular lens; CF: counting fingers

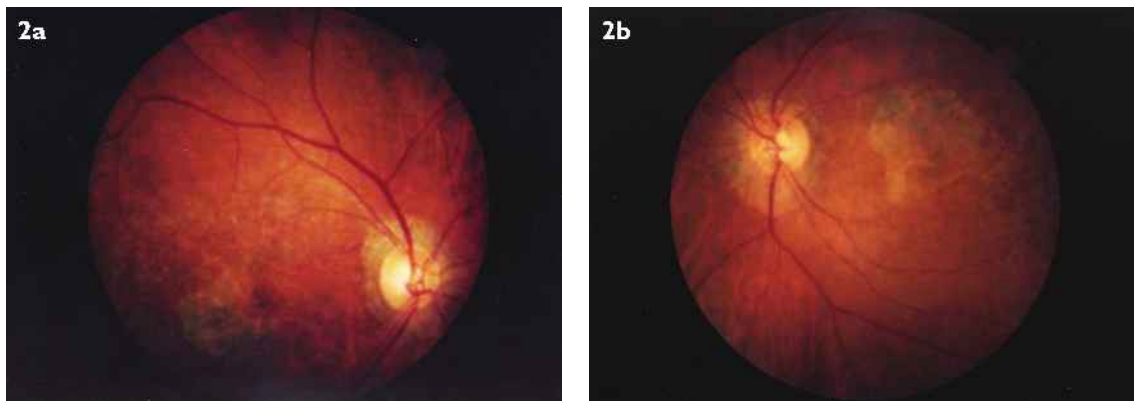
There were 50 cases in 1991 and 64 in 1992, with a yearly average of 57 cases. There were 61 (53.5%) males and 53 (46.5%) females. The mean age of the patients was 67.5 years, with a range of 50–84 years. There were 96 Chinese (84.2%), five Malays (4.4%), seven Indians (6.1%) and six others (5.3%) (Table I). The mean follow-up was at 32 months, with a range of 0–96 months.

There were 41 (21.8%) eyes with drusen alone, 39 (20.7%) with dry AMD and 108 (57.5%) with exudative AMD (Table I). The morphology of AMD was similar among the genders as well as among the Chinese and non-Chinese. The best-corrected Snellen visual acuity at presentation and at the final visit is represented in Table

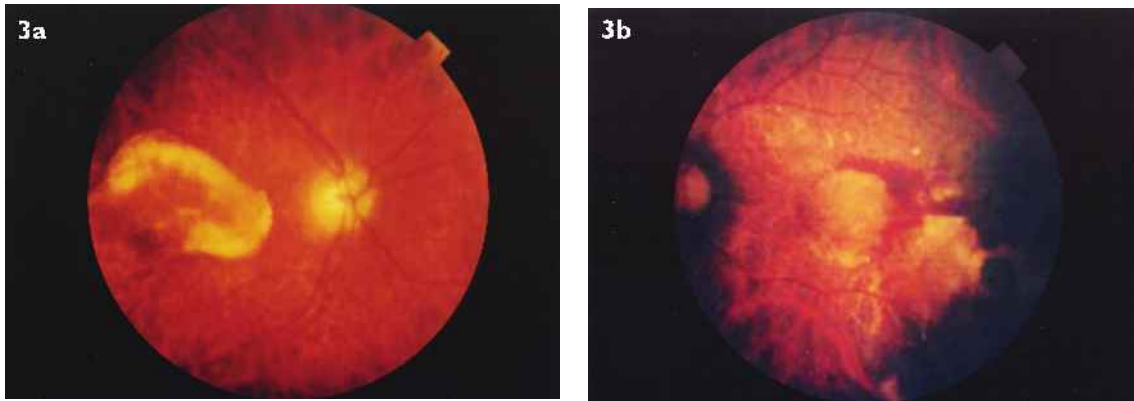
I. 116 (61.7%) of the patients' eyes had no change in visual acuity between presentation and final acuity, 14 (7.4%) had better visual acuity and 58 (30.9%) had worse visual acuity at the final visit. When compared between the three categories, patients with drusen alone tended to have better visual acuity as compared to patients with dry or wet AMD. A significant majority of the patients with dry (61.1%) and exudative (63%) AMD had legal blindness of 6/60 or worse at presentation ( $p < 0.0001$ ). Patients with dry AMD or drusen alone also tended to have the same or worsening visual acuity over time. On the other hand, 27 (33%) patients with exudative AMD had improved visual acuity over time.



**Fig. 1** Case 1. Photographs show exudative age-related macular degeneration. (a) OD: subretinal haemorrhage and exudates in posterior pole; and (b) OS: extra-foveal CNV.



**Fig. 2** Case 2. Photographs show dry age-related macular degeneration. (a & b) OU: geographical atrophy.



**Fig. 3** Case 3. Photographs show exudative age-related macular degeneration. (a) OD: disciform scar at macula; and (b) OS: pigment epithelial detachment with subretinal haemorrhage and exudates.

The characteristics and progression of five randomly-selected patients with different AMD morphology are shown in Table II. Cases 1, 3 and 4 had bilateral exudative AMD. Case 2 had dry AMD while Case 5 had right exudative AMD and left soft drusen. The two-year hospital incidence rate of AMD in 1991–1992 was 0.38% or equivalent to 3.8 per 1,000 new cases seen.

**DISCUSSION**

Data on the population-based incidence/prevalence of AMD in Asia was sparse previously. It was only in the

1990s that there were more reports on this disease in Asia. Most of the series quoted a population-based prevalence rate that is lower than reported among whites. In a population-based survey of subjects older than 40 years of age in Mongolia in 1991 and 1992, the prevalence of low vision was 8.1%, with 0.8% attributable to macular causes.<sup>(6)</sup> In a study of the visually handicapped in Tokyo, the prevalence of macular degeneration among them was 3.3% in 1998.<sup>(7)</sup> In a recent study by Oshima et al among residents of Hisayama, Fukuoka, Japan, the prevalence of any form of late age-related maculopathy in patients aged

50 and older was 0.87%, that of neovascular AMD 0.67% and that of geographic atrophy 0.20%.<sup>(2)</sup>

In a nationwide epidemiological survey of exudative AMD in Japan, the number of people visiting ophthalmology departments due to exudative AMD was 53 males and 20 females per 100,000 population aged 50 years or older.<sup>(5)</sup> On the other hand, the incidence and prevalence rate of AMD in the Western countries seem to be higher. In a Maryland population-based survey in 1985,<sup>(8)</sup> the age-specific prevalence rate of AMD for men aged 50–70 years was 35%, and 45.7% in men above 70 years of age. The incidence of visually-significant AMD, such as geographical atrophy and exudative AMD, is much lower. In the Beaver Dam Eye Study, the five-year incidence of geographical atrophy was 0.2%, exudative AMD 0.4% and the incidence of drusen was 42.8%.<sup>(9)</sup> Comparisons across studies, however, are limited by differences in definitions of AMD, selection of the study population and non-participation rates.

The two-year incidence of exudative AMD seen in Singapore in 1991 and 1992 was estimated to be 0.04%. This is an underestimate, as not all patients with exudative AMD would present to the hospitals. However, most patients with exudative AMD would have presented to the hospital as a result of the significant visual degradation. The incidence of exudative AMD in Singapore is about 4.5 times more than the incidence of geographical or dry AMD. This higher incidence is in contrast to the Beaver Dam Eye Study where the incidence of wet AMD is twice that of geographical atrophy.<sup>(9)</sup> This apparently higher incidence rate of exudative AMD may be due to the more significant visual degradation resulting in more of them seeking medical attention. However, it is our clinical impression that the incidence of geographical atrophy is less than that of exudative AMD.

The visual acuity at presentation is worse in the exudative AMD category, as compared to the dry AMD or drusen alone category. This can be attributed to the presence of submacular haemorrhage, exudates or glial tissue commonly found in exudative AMD. Over time, the submacular haemorrhage and exudation may be resolved, leading to improved vision. This accounts for the improved visual acuity in 27 (33.3%) of the patients in this category. Improvement of visual acuity is rarely reported in eyes with exudative AMD. It is possible that a significant proportion of eyes with exudative AMD in our population have idiopathic polypoidal choroidovasculopathy (IPCV),<sup>(10)</sup> which has a better prognosis than exudative AMD, hence accounting for the apparent improvement in visual outcome over time. Kwok et al, in a recent study of Chinese patients with

IPCV, found that stable or improved vision was attained in 56% and 31% of laser treated and non-laser treated groups, respectively.<sup>(11)</sup> This is very different from the poorer visual prognosis described in late forms of exudative AMD.

There is no significant gender difference in the pattern of the morphology and presentation of AMD. This finding is in contrast to previous studies in Japan, which showed a consistently higher number of males with exudative AMD.<sup>(2,3)</sup> On the other hand, the Beaver Dam Eye Study and the Blue Mountains Eye Study showed a higher prevalence of exudative macular degeneration in women compared with men at age 75 years and older.<sup>(9,12,13)</sup> This may be due to ethnic and racial differences between the different study groups.

There are limitations to this study as it is retrospective in nature. Some AMD cases may have been miscoded and missed in the initial data collection. As this study only involves hospital cases, the calculated population incidence rate would be an underestimate of the true incidence. In order to calculate the population-based incidence rate of exudative AMD, we have made several assumptions: AMD patients and cataract patients are similar in age and visual presentation. The probability of an AMD patient presenting in any of the eye institutions in Singapore is the same as a cataract patient. This hospital therefore had the same proportion of patients compared to the total number of patients in Singapore with respect to cataract and AMD. Patients with exudative AMD tend to present to an eye institution, as most of them would have a significant visual complaint.

In conclusion, the estimated population incidence rate of exudative AMD in 1991 and 1992 in Singapore is found to be 0.04%. Although this rate is lower than that of the Western population, it is nonetheless a significant cause of visual loss. A significant majority of patients with dry and exudative AMD had legal blindness at presentation ( $p < 0.0001$ ). Notably, 33.3% patients with exudative AMD had improved vision over time, in comparison to a majority of patients with dry AMD or drusen alone who tended to have the same or worsening visual acuity over time. The proportion of exudative AMD to geographical atrophy appears to be higher than in Western studies.

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