Baseline Macular Pigment Optical Density among Filipinos with Age-related Macular Degeneration

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ABSTRACT

Objective: To compare the macular pigment optical density (MPOD) among Filipinos with and without age-related macular degeneration (AMD).

Methods: Consecutive patients with AMD and without posterior segment disease were recruited into the study Baseline MPOD measurements using an autofluorescence spectrometer were obtained. MPOD in the 0.5 degree retinal eccentricity and the average of 3 measurements (MPOD Max) was the primary outcome measure.

Results: 120 patients, aged 50 to 80 years, were included into 3 groups: group 1 (n=40) without retinal disease, group 2 (n=40) with non-neovascular AMD, and group 3 (n=40) with neovascular AMD. The mean baseline MPOD were: 0.382 ± 0.10 DU for group 1, 0.333 ± 0.07 DU for group 2, and 0.283 ± 0.07 DU for group 3. Significant differences were present comparing the MPOD values of the 3 groups.

Conclusion: Eyes without retinal disease had higher MPOD than those with early non-neovascular or neovascular AMD.

Key Words: Macular pigment optical density, Age-related macular degeneration, Neovascular AMD

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Age-related macular degeneration (AMD) is a progressive maculopathy, with no definitive treatment.[1]

The disease is frequently encountered in the elderly and is the leading cause of visual and functional impairment in those older than 65 years. Conversely, AMD is less common in younger individuals. Several studies have determined the prevalence of AMD among those younger than 55 years old to be 6.4 to 10%, escalating to 19.7 to 36.8% among individuals older than 75 years.[2-6] Moreover, racial differences are thought to affect AMD prevalence, as studies have consistently reported that AMD is less frequent among Africans and African-Americans compared to Caucasians.[5]

It has been proposed that racial differences in macular pigment levels, as well as differences of younger compared to older patients, may be related to the incidence of AMD.[5]

Recently, it has become possible to objectively measure the concentration of macular pigments in the retina, also known as the macular pigment optical density (MPOD).[7] Because of this, effects of dietary supplements on macular pigmentation are now quantifiable.[8] In addition, differences in spatial distribution of the macular pigment can be compared among eyes with and without AMD.[9] Likewise, the changes in MPOD may be documented and measured to determine which eyes may be more susceptible to future development and/or deterioration of AMD.[2]

Racial differences in MPOD have been reported, with the general trend of higher MPOD values among blacks and Asians compared to Caucasians.[9-20] Hence, it is useful that normative values for MPOD specific to Filipinos be determined to be used as baseline. Once these values are obtained, they can be compared across the ages and among eyes without retinal disease versus those with neovascular and non-neovascular AMD. In the future, modifications in macular pigment density may be used for earlier identification of patients at risk of developing early, non-neovascular AMD or eyes at risk for deterioration to late, neovascular AMD.

This study compared the MPOD among Filipinos with and without AMD.

METHODOLOGY

Study Design and Sampling

Consecutive sampling of patients without retinal disease and those with neovascular and non-neovascular AMD was done. They were recruited from the patients consulting at the out-patient section of the Philippine General Hospital, Department of Ophthalmology and Visual Sciences. After approval from the University of the Philippines Manila Research Ethics Board was obtained, data collection took approximately 12 months, starting from August 2013 until August 2014. Of the 123 patients recruited, 120 successfully completed the study (N=120).

The participants were divided into three groups (40 per group). Detailed description and differentiation of each group is presented in Table 1.

Table 1. Grouping classification and criteria based on Age-Related Eye Disease Study report.[1]

Group	Drusen size	Pigment abnormalities	Fellow eye
Without retinal disease	None	None	None
Non-neovascular AMD	Small (≤63 um), intermediate, or large (≥125 um)	Absent or present but central geographic atrophy absent	Same findings
Neovascular AMD	Any size	Absent or present with central geographic atrophy and features of advanced AMD: photocoagulation or other treatment for choroidal neovascularization, non-drusenoid retinal pigment epithelial detachment, serous or hemorrhagic retinal detachment, hemorrhage under the retina or the retinal pigment epithelium, subretinal fibrosis	Same or as described in category 2-3

AMD – age-related macular degeneration

Patients who were between 50 and 80 years of age with no history of beta-carotene intake in the last 6 months prior to inclusion into the study were

recruited. Additional criteria included diagnosed cases of AMD for group 2 or 3 or no posterior segment disease for group 1.

Those with a history of prior intraocular surgery including intravitreal injections and posterior segment laser treatment, those not willing to go to the Manila Medical Center for MPOD measurement, and those not willing to give informed consent were excluded.

Data Collection and Outcome Measurement

After the initial ophthalmologic evaluation, participants were brought to another testing site for MPOD measurements using the Zeiss Visucam 500 via autofluorescence spectrometry. The autofluorescence of the fundus at differing wavelengths were captured on video frames. Digital subtraction of the reflectance maps at 488 and 514 nm, with adjustments made for absorption by the lens, yielded the mean macular pigment density.[7] Two orthoptists who used the same testing device conducted all the measurements. Interrater reliability scans were obtained at the start of the study. Repeat measurements of MPOD were performed until 3 values with 0.02 density unit (DU) difference were obtained. The average among the 3 measurements was taken as the MPOD Max.

The primary outcome measure was the MPOD obtained in the 0.5 degree retinal eccentricity or MPOD Max on autofluorescence measurement.

For group 1 (without retinal disease), the eye with the better visual acuity was selected as the study eye. If visual acuity was similar between the 2 eyes, the right eye was selected.

For groups 2 and 3 (with non-neovascular and neovascular AMD respectively), the eye with findings consistent with AMD was selected as the study eye. If both eyes were affected, the right eye was selected.

Statistical Analysis

Data were analyzed using IBM - SPSS version 19.0 program for statistical analysis. One-way analysis of variance (ANOVA) was used to compare the baseline MPOD values of the 3 groups.

RESULTS

The baseline demographics of the 120 participants, 40 in each group, are shown in Table 2.

Table 2. Baseline demographics of the study participants (N=120).

Group	n	Age	Sex
Group 1 (without retinal disease)	40	Range: 52-80 Mean: 64.25	Female: 35 Male: 5
Group 2 (with AMD non-neovascular)	40	Range: 50-80 Mean: 65.78	Female: 20 Male: 20
Group 3 (with AMD neovascular)	40	Range: 58-80 Mean: 68.55	Female: 21 Male: 19
p value		p = 0.052	p = 0.876

*significant p <0.05

The mean ages for groups 1, 2, and 3 were 64.25, 65.78, and 68.55 years, respectively. The participants from group 3 were slightly older compared to the other 2 groups; the difference, however, was not significant (p=0.052).

There were more females than males recruited in group 1. For groups 2 and 3, the numbers of females and males were comparable. Comparison of sex among the 3 groups showed no significant difference (p=0.867).

Baseline Macular Pigment Optical Density

The baseline MPOD obtained for each group is presented in Figure 1. The mean baseline MPOD were: 0.382 ± 0.01 DU for group 1; 0.333 ± 0.07 DU for group 2; and 0.283 ± 0.07 DU for group 3. One-way ANOVA post-hoc analysis using Tukey test, comparing one group to another, showed that the mean difference in baseline MPOD between group 1 and group 2, between group 2 and group 3, and between group 1 and group 3 were all significant (Table 3).

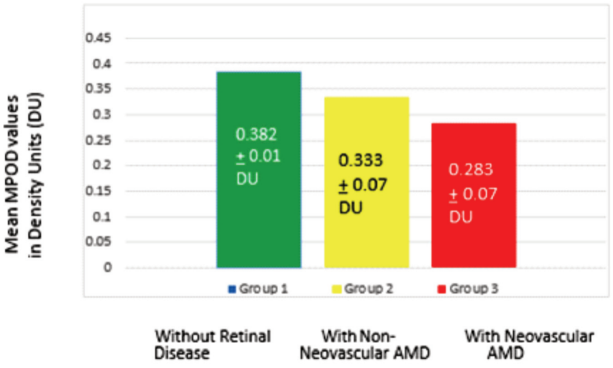

Figure 1. Comparison of MPOD at baseline.

Table 3. Between groups comparison of baseline MPOD.

Between Groups Comparison	Mean Difference (Density Unit)	p value
Group 1 vs Group 2	0.048 ± 0.018 DU	p = 0.021*
Group 1 vs Group 3	0.099 ± 0.018 DU	p = 0.001*
Group 2 vs Group 3	0.050 ± 0.018 DU	p = 0.017*

Group 1: without retinal disease
Group 2: with non-neovascular AMD
Group 3: with neovascular AMD
*Significant p value <0.05

DISCUSSION

This was a comparative non-randomized study comparing the baseline MPOD of Filipinos without retinal disease; with early, non-neovascular AMD; and with late, neovascular AMD.

Our results suggested that the baseline macular pigments as measured by MPOD of eyes without retinal disease were significantly higher than those of AMD patients (p=0.021 for non-neovascular and p=0.001 for neovascular AMD). Furthermore, the baseline MPOD of patients with early, non-neovascular AMD were significantly higher than those with late, neovascular AMD (p=0.017). These results were consistent with previous studies.[16,21,22]

Higher MPOD among patients without retinal disease reflected higher content of lutein and zeaxanthin, which have been reported to act as filters to damaging short wavelengths.[23] Lutein and zeaxanthin limit oxidation of phospholipids originating from spent photoreceptor outer segments, and to subsequently protect from drusen formation.[24-27] They exert their antioxidant properties by scavenging reactive oxygen species and reducing lipofuscin synthesis and accumulation.[24,28-30] Lutein and zeaxanthin absorb approximately 40% of the shorter blue wavelengths before they reach the photoreceptor and retinal pigment epithelium layers.[31] A study from Bone et al[32] showed that people with low MPOD have retinas that were exposed six times more to short wavelength-blue light compared to those with higher percentiles of MPOD. This study also showed that in non-neovascular AMD with geographic atrophy, the foveal center of those at the highest quintile of MPOD were spared, and that these eyes were among the last to show changes consistent with late, neovascular AMD.[32] This protective effect of high MPOD was also seen in the Eye Disease Case-Control Study Group (EDCCSG) which reported significant associations between high levels of lutein and zeaxanthin in both the diet and serum of their subjects, and a reduced risk of advanced, neovascular AMD.[10] Studies also suggested that patients with high MPOD, such as in the normal group of this study, may have a lower risk of developing AMD.[6,33]

This study utilized the Carl Zeiss Meditec's Visucam 500, which employs the principle of autofluorescence in MPOD measurement. Fundus autofluorescence utilizes reflectance maps made by different cells in the retina. Digital subtraction of the reflectance maps at 488 and 514 nm, with adjustments made for absorption by the lens, yields the mean macular pigment density.[7] Table 4 shows the MPOD values of this study compared to other studies that used the same method.

The mean MPOD from this study was lower than those obtained from other studies with Asian participants (Japanese and Singaporean-Chinese). However, it was higher than the mean MPOD obtained from studies with Caucasian participants. This finding was consistent with results of other studies that showed an association between ethnicity and MPOD values.[11,12,34] The mean MPOD in this study was also higher than the values found in another local study; however, a different method of measurement was used.

Table 4. Comparison of MPOD values of studies utilizing autofluorescence among patients without retinal disease.

Study	Method of MPOD measurement	Sample	MPOD values at baseline
Santos, Cubillan, 2014	Autofluorescence using Carl Zeiss Visucam 500	Healthy Filipino N=40 Age: 52-80 (mean 64.25)	0.382±0.01 DU
Neelam, Ho et al, 2014	Autofluorescence using Carl Zeiss Visucam 500	Healthy Singaporean-Chinese N=150 Age: 42.40±13	Females: 0.52±0.17 DU Males: 0.61±0.2 DU (p = 0.03)
Sasomoto, Gomit, et al, 2011	Autofluorescence using Carl Zeiss Visucam 500	Healthy Japanese N=43 Age: 64.5±9.1	0.480±0.136 DU
Kanis, 2007[16]	Spectral fundus reflectance	Caucasian N=435	0.33±0.15 DU
Trieschmann, et al, 2007[19]	Autofluorescence using Carl Zeiss Visucam 500	Healthy Caucasian N=147 Age: 50-80	0.380±0.4 DU
Study from University of Santo Tomas, 2012 (unpublished)	Heterochromatic flicker photometry	N=156 eyes	0.321±0.075 DU

In summary, eyes without retinal disease had higher MPOD values than those with early, non-neovascular or neovascular AMD. There are racial differences in MPOD values and obtaining normative MPOD for Filipino eyes without retinal disease is important. Future studies on larger samples are needed to establish the normative database.

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