Original Article

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Macular Pigment Optical Density and its Determinants among Adults: A Cross-sectional Study

Ophthalmology Section

POOJA GOYAL[1], MITASHA SINGH[2], SHASHI VASHISHTH[3], SATISH JAYERIA[4]

ABSTRACT

Introduction: Interplay exists between the risk factors of Age-related Macular Degeneration (AMD) and the factors influencing Macular Pigment Optical Density (MPOD) level. Early diagnosis and antioxidants supplementation is the only intervention which may possibly slow down the macular degeneration.

Aim: To measure MPOD and study the possible risk factors associated with subnormal MPOD among adults patients attending Outpatient Department (OPD).

Materials and Methods: A cross-sectional study was conducted among patients aged 20 years and above who visited Ophthalmology OPD in a tertiary care centre during the month of August (between 1st to 31st) 2018. Only those having Best-Corrected Visual Acuity (BCVA) better than 6/60 were enrolled for the study. MPOD was measured using a macular densitometer (Macular Matrics II, USA). Patients found to have subnormal MPOD further underwent Optical Coherence Tomography (OCT) and fundus. Fischer's-exact and Chi-square tests were applied wherever applicable; differences were considered to be statistically significant at p-value <0.05.

Results: A total of 82 patients participated in the present study. Total of 45.1% participants were found to have subnormal MPOD using macular densitometer. Prevalence was least among <30 years of age (nil) and maximum after 50 years (58.8%) (p<0.05). Trends revealed that subnormal MPOD was more frequent among smokers (p-value=0.13), vegetarians (p-value=0.38) and those who were malnourished (under or over weight) (p-value=0.15), though not found to be statistically significant. Non-modifiable risk factors, an inverse relationship was observed between age and MPOD levels.

Conclusion: The study noted associations between subnormal MPOD and multiple risk factors, several of which are modifiable factors. These modifiable risk factors included smoking and malnourishment.

Keywords: Age-related macular degeneration, Macular densitometer, Screening

INTRODUCTION

Macular pigment (MP) is the pigment composed of three carotenoids, lutein (L), zeaxanthin (Z), and *meso*-zeaxanthin (*meso*-Z), that accumulates at the macula [1,2]. In humans, L and Z cannot be synthesised de novo and are derived entirely from diet, whereas *meso*-Z is largely derived from retinal L [1,2]. It is believed that MP may afford protection against the development of Age-Related Maculopathy (ARM) due to its short-wavelength light screening and antioxidant properties [1]. A study has documented the association of MPOD with risk factors for AMD in Irish subjects and reported that there is a relative lack of macular pigment in association with the risk factors for AMD [3].

Globally, AMD ranks third as a cause of blindness after cataract and glaucoma. It accounts for 8.7% of the total blindness globally and is the primary cause of visual impairment in industrialised countries [4]. Out of its two forms- dry and wet, later one is less common but much more serious as loss of vision is faster with wet AMD [5]. At present, there is no definite treatment available. Early cases of AMD can possibly be slowed down with antioxidants like lutein and xeaxanthin in diet and/or taken as supplements [6]. Screening of AMD at an early age may possibly limit disability and inturn reduce disability adjusted life years. Possible risk factors for AMD that had been identified in earlier studies are non-modifiable such as age, gender and genetic predisposition [4,7-10] and modifiable such as sun exposure, smoking, systemic hypertension, and dietary habits [9,11-15]. There exists interplay between the risk factors of AMD and the factors influencing MPOD level. There is evidence of increasing age, smoking, ultraviolet exposure, and obesity influencing the AMD, as well as the levels of MPOD [3,16-20].

A variety of techniques can be used to estimate the Macular Pigment; Heterochromatic Flicker Photometry (HFP), fundus reflectometry, fundus auto fluorescence, and resonance Raman spectroscopy [21]. In the present study, MPOD was measured by means of a macular densitometer. It is a non invasive technique available to estimate the level of macular pigments in eye. As per available literature, this test does not require pupil dilation [22]. Also, results are available to the doctor within a short time for review. Hence, present study was planned to measure Macular Pigment Optical Density (MPOD) and to study possible risk factors associated with subnormal MPOD.

MATERIALS AND METHODS

It was a cross-sectional study conducted among all the patients who visited Ophthalmology OPD at a ESIC Medical College and Hospital, tertiary care center, Faridabad, Haryana between 1st to 31st August, 2018. The study was duly approved by the Institutional Ethical and Research Committee (vide no. 134/A/11/16/Academics/MC/2016/155). Informed written consent was obtained from each participant.

Study period was short as a macular densitometer was installed in the Ophthalmology Department for a limited period by Vekaria Healthcare, a company dealing with medical devices.

Inclusion and Exclusion criteria: Patients aged 20 years and above were included in the study. Only those having BCVA better than 6/60 were enrolled for the study. Patients with significant media opacity interfering with fundus examination and MPOD measurement and those who were not willing to participate were excluded from the study. A total of 82 participants were included in study.

Study Tool and Data Collection

A self-designed questionnaire was piloted on ten random people from the OPD and was also evaluated by ophthalmology experts. It comprised of following sections- socio-demographic profile, risk factors for ARMD (age, gender, smoking history, dietary habits, sunlight

exposure history), physical examination and ocular examination including vision status, refraction, color vision, fundus examination and macular densitometry was used. The same questionnaire with minor changes in language of some questions (as suggested by experts) was used for data collection. The data collection was done by the ophthalmology residents in OPD setting through interview technique.

For measurement of sunlight exposure, participants were asked about their residence and job history including time spent outdoors as well as in homecare throughout their working life. Also, information on the use of hats and eyewear (glasses, contact lenses, and sunglasses) was obtained. Persons smoking atleast one pack of cigarettes/day for the last one year were considered as smokers in the present study. Body Mass Index (BMI) of all the participants was measured and using World Health Organisation (WHO) criteria, subjects were classified into underweight (BMI, <18.5), normal (BMI,18.5- 24.9), overweight/pre-obesity (BMI, 25-29.9) and obese (BMI, 30 or more) [22]. Fundus examination and MPOD estimation using macular densitometer was done in all the study participants. MPOD was measured using a macular densitometer (Macular Matrics II, LLC, Rehoboth, Massachusetts, USA) which uses psychophysical method of HFP {in Density Units (DU)}.

Unilateral MPOD was evaluated and the eye to be tested for the present study was selected randomly based on the random number tables. The measurement was performed before pupil dilation under non-mydriatic conditions among all the study subjects. The participants viewed a small test field superimposed on a blue-background. The test field alternates between a wavelength (blue or blue-green) that is absorbed by the macular pigment and a reference (green to yellow-green) wavelength that is outside the absorption band of macular pigment. When the frequency of alteration is chosen correctly, the test field appears to flicker [23]. The basic assumption underlying the method is that the spectral sensitivities of the visual mechanism detecting the stimulus in the fovea and parafovea are the same [23]. The technique requires subjects to have good cognitive function and certain level of intelligence to understand instructions to be followed during test.

All MPOD measurements were made by a single technician who was appointed by the company named Vekaria Healthcare to avoid inter observer bias. Specific instructions imparted to the patients and recording of MPOD values was performed by the same technician throughout the data collection. As the instructions to the subject must be clear, simple, and often repeated so training of the examiner in techniques to explain procedures and to motivate the subject is likely to be important in obtaining reliable measurements.

Fundus examination was done after dilating the pupil with the eye drop containing combination of tropicamide 0.8% and phenylepherine 5% [24]. Fundus was said to be abnormal in case of drusen, hypopigmentation, hyperpigmentation and absent fovea reflex [25]. OCT and fundus photography was performed among only those patients having subnormal MPOD as detected by macular densitometer.

STATISTICAL ANALYSIS

Data was analysed using commercially available statistical software (IBM SPSS version 21). Results were expressed as absolute numbers and percentages. Based on the mean value of MPOD recorded on the equipment, subjects were classified into two categories i.e., having subnormal MPOD (<0.4) and normal MPOD (≥0.4). Fischer's-exact and Chi-square tests were applied wherever applicable; differences were considered to be statistically significant at p-value <0.05. Pearson's correlation coefficient was calculated to study correlation between the risk factors and MPOD values.

RESULTS

A 58.5% participants enrolled in the study were between 20 to 50 years of age and rest 41.5% were above 50 years. Gender distribution was more or less equal with slight female preponderance (53.7%). Half of the participants were strict vegetarians and others were having mixed dietary habits [Table/Fig-1].

Variable	Males n (%)	Females n (%)	Total n (%)
Age (years)	38 (46.3)	44 (53.7)	82 (100.0)
21-30	2 (40.0)	3 (60.0)	5 (6.1)
31-40	6 (28.6)	15 (71.4)	21 (25.6)
41-50	11 (50.0)	11 (50.0)	22 (26.8)
>50	19 (55.9)	15 (44.1)	34 (41.5)
Dietary habits			
Vegetarian	18 (43.9)	23 (56.1)	41 (50.0)
Mixed	20 (48.8)	21 (51.2)	41 (50.0)

[Table/Fig-1]: Distribution of subjects according to their socio-demographic profile and dietary habits (N=82).

Based on the measurement of MPOD using a macular densitometer, 45.1% participants were found to have subnormal MPOD whereas 54.9% were having normal macular optical density.

Mean age of the participants was found to be 46.45 years (SD, 11.68) and the range varied from 21 to 69 years. Prevalence of subnormal MPOD was least (nil) among participants below 30 years of age and maximum after 50 years (58.8%). Results of the present study revealed that the risk of subnormal MPOD increases with the advancement of the age (p=0.05) [Table/Fig-2].

	MPOD				Total		p-value
	<0.40 (n=37)		≥0.40 (n=45)				
Risk factor	n	%	n	%	N	%	
Age (Years)							0.05*
21-30	0	0	5	100.0	5	100	
31-40	7	33.3	14	66.7	21	100	
41-50	10	45.5	12	54.5	22	100	
>50	20	58.8	14	41.2	34	100	
Gender							0.66#
Male	16	42.1	22	57.9	38	100	
Female	21	47.7	23	52.3	44	100	
Dietary habits							0.38#
Vegetarian	21	51.2	20	48.8	41	100	
Mixed diet	16	39.0	25	61.0	41	100	
Past history of ocular surgery							0.29*
Present	6	66.3	3	33.3	9	100	
Absent	31	42.5	42	57.5	73	100	
Exposure to sunlight (hours)							1.00#
>4 hours	5	45.5	6	54.5	11	100	
<4 hours	32	45.1	39	54.9	71	100	
Smoking							0.13#
Present	8	66.7	4	33.3	12	100	
Absent	29	41.4	41	58.6	70	100	
BMI (Kg/m^2)							0.15#
<18.5	5	71.4	2	28.6	7	100	
18.5-24.9	14	45.2	17	54.8	31	100	
25-29.9	13	35.1	24	64.9	37	100	
30 or more	5	71.4	2	28.6	7	100	

[Table/Fig-2]: MPOD and its associated risk factors among study subjects (N=82). #Fischer-exact test; *Chi-square test; BMI: Body mass index; p-value <0.05 considered significant

Subnormal MPOD values were higher among females (47.7%), smokers (66.7%), vegetarians (51.2%), those who underwent some ocular surgery in the past (66.3%) and who were overweight or underweight according to their BMI. However, the differences between the two groups were not statistically significant (p>0.05) [Table/Fig-2]. Age was inversely correlated with MPOD and was statistically significant. (r=-0.223, p=0.044) [Table/Fig-3].

Risk factors	Pearson's correlation coefficient	p-value
Age	-0.223	0.044*
Sex	-0.014	0.902
BMI	0.405	0.093
Smoking	0.107	0.340
Type of diet	0.105	0.347
Sunlight exposure	-0.084	0.452

[Table/Fig-3]: Correlation between various risk factors and MPOD.
*p-value less than 0.05 is considered statistically significant

DISCUSSION

The study subjects were classified into two categories (<0.40 and ≥0.40) based on estimated MPOD values by a macular densitometer. Total 45.1% participants were found to have subnormal MPOD and rest was having normal MPOD. Present study observed an inverse relationship between age and MPOD. Risk of reduced MPOD rises with increasing age. Subnormal MPOD was observed to be nil among participants below 30 years of age and maximum after 50 years. Jahn C et al., also observed that there is a weak negative correlation between age and MPOD [26]. The majority of HFP techniques used reference points at 5° eccentricity (taken as a zero reference point); it is likely that such techniques result in underestimation of peak MPOD [16]. Also, with age, there is an extension of the lateral extent of MP, which can be a reason for the studies with HFP showing an age-related decline in MPOD [27].

Subnormal MPOD was higher among females as compared to males, though this difference was statistically non-significant. Kulkarni SR et al., Pokharel S et al., and Hazin R et al., in their study have also reported higher female preponderance [4,28,29]. However, study by Ji Y et al., did not reported any sex specific predominance [30]. Female participants were not only higher in number but also their age-wise distribution revealed that more females were above 30 years of age as compared to males. This may be the possible reason for female preponderance in the present study.

Subnormal MPOD was more among smokers (66.7%) as compared to non-smokers in current study. Wooten BR and Hammond BR, and Raman R et al., has also reported that current cigarette smokers had less MPOD as compared to non-smokers [31,32].

Present study did not observe any association between long term exposure to sunlight and subnormal MPOD. Khan JC et al., in their study also reported the same [33]. MPOD was observed to be subnormal in 51.4% subjects who were vegetarian. A systematic review conducted by Chapman NA et al., states that quality of diet and food intake had a vital role in AMD but the same cannot be established in the present study due to lack of detailed nutrition history [34].

Though not statistically significant but trend observed was that subnormal MPOD was more common among those who underwent some ocular surgery like cataract in the past (66.3%) which is consistent with other studies by Klein R et al., Krishnaiah S et al., and Wang JJ et al., [7,11,15]. Higher risk was observed among overweight or underweight study participants. Inverse relationship between BMI and MPOD has been reported in two studies by Nolan JM et al., [3,35].

Limitation(s)

Small sample size due to availability of macular densitometer for a shorter period of time. Therefore, some of our non-significant findings may be true associations that were missed because of low power. The tertiary care hospital where the study was conducted caters only to the population covered under Employees State Insurance (ESI) scheme and having income less than 21,000/month. Hence, results pertained to a population having specific characteristics.

CONCLUSION(S)

Keeping modifiable determinants (smoking, BMI) of MPOD under control will help to prevent development of subnormal MPOD levels. Among the non-modifiable determinants, age was found to have an inverse relationship with MPOD levels.

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PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Community Medicine, ESIC Medical College and Hospital, Faridabad, Haryana, India.
2. Assistant Professor, Department of Community Medicine, ESIC Medical College and Hospital, Faridabad, Haryana, India.
3. Professor, Department of Ophthalmology, ESIC Medical College and Hospital, Faridabad, Haryana, India.
4. Assistant Professor, Department of Ophthalmology, ESIC Medical College and Hospital, Faridabad, Haryana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Mitasha Singh,
Department of Community Medicine, ESIC MCH, NIT, NH3, Faridabad, Haryana, India.
E-mail: mitasha.17@gmail.com

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PROFORMA

1. Name:
2. Age/Sex:
3. C.R. No:
4. Address:
5. Occupation

History:

1. Is there any problem in watching TV, reading newspaper, driving etc.,
   (a) Yes (b) No
2. History of laser or ocular surgery
   (a) Yes (b) No
3. Family history of ARMD
   (a) Yes (b) No
4. Exposure to digital devices/blue light
   (a) <4 hours (b) >4 hours
5. Sun exposure
   (a) Yes (b) No
6. History of smoking
   (a) Yes (b) No
7. Medical history- DM/HTN/Hyperlipidemia/any other
8. History of any dietary carotenoids prescribed by ophthalmologist
   (a) Yes (b) No
9. History of cataract surgery
   (a) Yes ((b) No
   If yes- Date of surgery:

EXAMINATION:

1. BP
2. Height (meter)
3. Weight (kg)
4. BMI
5. Skin complexion

OCULAR EXAMINATION:

Parameter	Right	Left
Visual acuity Refraction BCVA Contrast sensitivity Color vision Ocular adnexa Conjunctiva Cornea Anterior chamber Iris Pupils Lens Fundus Fundus photo MPOD IOP		

Final diagnosis: