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Demographic and clinical features of age related macular degeneration in patients attending Mansoura University Ophthalmic Center

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Short title*:* Demographic and clinical features of age related macular degeneration.

ABSTRACT

Purpose: evaluate the demographic characteristics and clinical features of Age Related Macular Degeneration in patients attending Mansoura University Ophthalmic Center.

Methods: Observational descriptive cross sectional study carried out in Mansoura Ophthalmic Center – Mansoura University on patients with age related macular degeneration during the period from November 2019 to October 2020.

All individuals were subjected to full history and ocular examination & assessed for age-related macular degeneration staging, demographic and clinical features.

Results: The study included 193 eyes of 105 patients with age related macular degeneration, they had been classified into three groups: Group I: 53.4% had drusen. Group II: 35.2% had Choroidal neovascularization. Group III: 11.4% had geographic atrophy. The mean of age group was 67.7 ± 9.32 and median was 68 years in our study, 69.01±9.706 for group I, 66.61±8.77 for group II, and 69.18±9.65 for group III. There were 66.7% females& 33.3% males. The most common disease among studied group was hypertension, followed by diabetes mellitus, and then hyperlipidemia. Regarding general risk factors, 59% were prolonged exposued to sun, and 32.4% were smokers. Nineteen patients (18.1%) had previous cataract surgery. Regarding refraction, 68.6% of patients had hypermetropia, 12.4% had myopia, and 19% were emmetrope.

Conclusion: there are some common demographic characteristics for AMD which considered as preventable risk factors like smoking, prolonged sun exposure, and hyperlipidemia. AMD was common in cases with DM, and HTN. Visual affection and central visual loss is more likely with geographic atrophy, then in wet AMD, and vision is less affected in cases with drusen.

Key words: Age related macular degeneration, Drusens, Choroidal neovascularization, Geographic atrophy.

INTRODUCTION

Age-related macular degeneration is one of the common leading causes of blindness worldwide in older patient population[1]. The growing trend of population aging will increase the burden of age-related macular degeneration related ocular morbidity which results in dominant impairment in quality of life, emotional insult and functional independence[2].

About 90 percent of people diagnosed with macular degeneration have the dry form. Approximately 10 percent of people with macular degeneration have the wet type, which is a more progressive form of the disease [3].

Dry AMD most commonly results from a slowly progressive atrophy of the photoreceptors, RPE and choriocapillaris. It involves a variety of presentations including hard drusen, soft drusen, and geographic atrophy (GA) of the retinal pigment epithelium (RPE)[4]. Dry macular degeneration may affect both eyes, but vision can be lost in one eye without a change in the other eye).

The wet form is more aggressive than the dry type. If the leaking from these abnormal blood vessels is not controlled, it can lead to scarring and a permanent loss of central vision[3].

Drusen appear as yellow excrescences beneath the RPE, distributed symmetrically at both posterior poles. They may vary in number, size, shape, degree of elevation and extent of associated RPE changes[6]. Geographic atrophy secondary to AMD is currently defined by the presence of sharply demarcated atrophic lesions of the outer retina, resulting from loss of photoreceptors, RPE, and underlying choriocapillaris, leading to irreversible visual loss[7].

Wet AMD, is a less common but more severe form of AMD. Although wet AMD only accounts for about 10% of the overall AMD incidence, it is responsible for 90% of cases of severe vision loss[8]. In wet AMD, choriocapilaries complex are almost completely lost, become hypoxic and produce hypoxia-inducible growth factors, including vascular endothelial growth factor that induce formation of choroidal neovascularization (CNV), penetrating Bruch's Membrane and RPE[9].

There are many risk factors for AMD like age, sex, ethnicity, prolonged exposure to sun, and some systemic disorders as DM, HTN, and hyperlipidemia. The highest risk of developing of Age-related macular degeneration is in the population older than 65 years[2].

Female sex has been reported as a risk factor, some studies suggest that female sex is associated with a higher progression rate from early to late AMD[10].

Sunlight exposure is thought to result in more oxidative stress in the retina, causing the development of AMD[11]. Smoking is the most consistently reported modifiable risk factor for AMD and is associated with a 2–4 folds increased risk for any form of AMD[12]. Hyperlipidemia is mostly associated with AMD than other systemic diseases[13]. Visual affection and central visual loss is more with geographic atrophy, then in wet AMD, and vision is less affected in drusen cases[14].

Diagnosis of age-related macular degeneration can be done by fundus examination and imaging procedures including fundus fluorescein angiography, optical coherence tomography & optical coherence tomography angiography[15].

This study aims to evaluate the demographic characteristics and clinical features of Age Related Macular Degeneration in patients attending Mansoura University Ophthalmic Center.

PATIENTS AND METHODS

This was an observational descriptive cross sectional study carried out in Mansoura Ophthalmic Center – Mansoura University on patients with age related macular degeneration during the period from November 2019 to October 2020.

Inclusion criteria:

Patients 50 years, or older with age related macular degeneration.

Exclusion criteria:

1. Patients with other chorio-retinal diseases such as retinitis pigmentosa, vascular disorders.
2. Patients with previous treatment for AMD such as anti-VEGF injection, LASER therapy.
3. Opacities preventing fundus assessment.

Methods:

Assessment was done including:

History taking:

Including; age, sex, residency, history of smoking, medical history, social history, previous ocular trauma or surgery.

Examination:

Full ophthalmic examination was done including:

1. Visual acuity: Uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA) using Landlot's chart where results will be converted to log MAR chart values.
2. Slit lamp examination: To evaluate anterior segment of the eye.
3. Measurement of intra-ocular tension: using Goldmann applanation tonometry.
4. Fundus examination: by slit lamp with +90 Volk lens and indirect ophthalmoscopy.

Investigation:

1- Fundus photography.

2- Fundus fluorescein angiography

3- Optical Coherence Tomography

4- laboratory investigations: blood sugar, and lipid profile.

Ethical consideration:

- This study had been approved by Institutional Research Board code number MS.19.10.854, faculty of medicine, Mansoura University.
- Adequate provisions had been made to ensure the confidentiality of participant's data.

All data from patients' history, examination and investigations were reported in patient sheets.

Statistical analysis of data:

Results were statistically analyzed by using statistical package of social sciences (SPSS 27.0, IBM/SPSS Inc., Chicago, IL) Two types of statistical analysis were conducted.

Descriptive statistics:

It included estimates for summarizing the continuous data as mean (X) and standard deviation (SD) or median (Med) and range (IQR) for skewed data. Frequency with percentage (%) was used for presenting qualitative data.

Analytical or inferential statistics:

- **Pearson Chi-square (χ2) test:** It was used to compare between two or more groups regarding one qualitative variable.
- **Monte-Carlo test:** It was used instead of Chi-Square (χ^2) test when the assumption that at least 80% of the expected frequencies are greater than five was violated.
- **Analysis of variance (ANOVA or F test):** One-way ANOVA test was used for continuous data to test for significant difference between more than two normally distributed groups.
- **Kruskal-Wallis test:** It is a non-parametric equivalent to ANOVA and used when ANOVA assumptions were violated to compare between more than two groups of skewed data.

RESULTS

This study included; 193 eyes of 105 patients with age related macular degeneration, there was 70 females (66.7%) & 35 males (33.3%) (Table.1). According to clinical history and risk factors in the cases of the study; The most common disease among studied group was hypertension (89.5%), followed by diabetes mellitus (53.3%), and then hyperlipidemia (42.9%). Regarding general risk factors, 59% of cases gave history of prolonged exposure to sun, and 32.4% were smokers (Table 2, fig.1). Regarding ophthalmic history and examination in the cases of the study; Nineteen patients (18.1%) had previous cataract surgery. Regarding refraction, 68.6% of patients had hypermetropia, 12.4% had myopia, and 19% of were emmetrope (Table 3).

Comparing the demographic data within the studied groups according to age related macular degeneration staging (Table4); There was no significant difference between studied groups as regard age (P value = 0.186). The prevalence of age related macular degeneration was common in females than male in our studied group (P value < 0.001). The most common type of AMD was drusen only (78.6%) & second most common type was wet type (58.8%). Comparing the clinical history and risk factors among the studied groups according to age related macular degeneration staging (Table 5).

There was significant increase in number of smokers in cases with age related macular degenerations (p value < 0.001). There was significant increase in number of cases with hyperlipidemia in cases with AMD (p value =0.019). There was significant increase in number of cases who prolonged exposed to sun in cases with AMD (p value =0.024). There was significant increase in cases with DM in cases with AMD (p value =0.038). Regarding ocular examination of the studied groups according to age related macular degeneration staging. Hypermetropia was statistically significant in cases with AMD (p value < 0.001). Cataract surgery was not correlated with AMD (p value = 0.900). Regarding BCVA of the studied groups according to age related macular degeneration staging; There was statistically significance difference of BCVA among

studied group (p value < 0.001). The patients with dry type AMD (Drusens) had BCVA of median 0.48 Log MAR. The patients with wet type AMD had BCVA of median 1.19 Log MAR. The patients with dry type AMD (geographic atrophy) had BCVA of median 1.3 Log MAR (Table 6).

Table (1): Demographic data in the cases of the study

Items		Study subjects (N = 105)	
Age (years)	Mean ± SD	67.7 ± 9.32	
	Median (min-max)	68 (50-90)	
		Number	Percent
Male		35	33.3
Female		70	66.7

Continuous data expressed as mean±SD and median (range) & Categorical data expressed as Number (%)

Table (2): Clinical history and risk factors in the cases of the study

Items	Study subjects (N = 105)	
	Number	**Percent**
Hypertension	94	89.5
DM	56	53.3
Hyperlipidemia	45	42.9
Smoking	34	32.4
Prolonged exposure to sun	62	59

Continuous data expressed as mean±SD and median (range) & Categorical data expressed as Number (%)

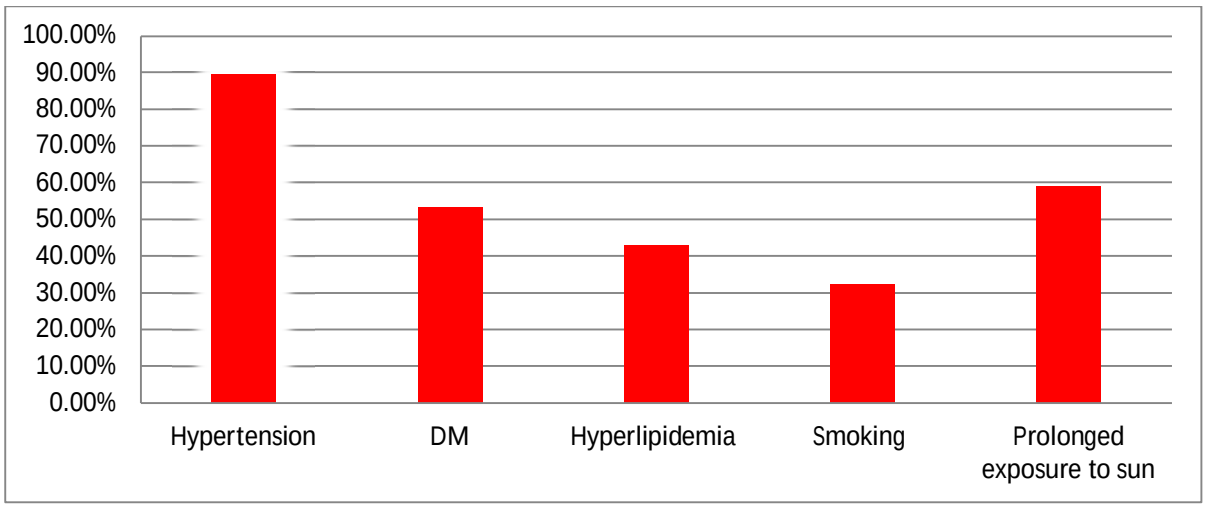

Figure (1): Clinical history and risk factors in the cases of the study

Table (3): Ophthalmic history and examination in the cases of the study

Items		Study subjects (N = 105)	
		Number	**Percent**
Previous ocular surgery		**19**	**18.1**
Refractive state	Emmetropic refraction	**20**	**19**
	Myopia	**13**	**12.4**
	Hypermetropia	**72**	**68.6**
OD BCVA	Mean ± SD	0.83 ± 0.49	
	Median (min-max)	0.78 (0.18 -1.78)	
OS BCVA	Mean ± SD	0.81 ± 0.45	
	Median (min-max)	0.78 (0 -1.78)	

Continuous data expressed as mean±SD and median (range) & Categorical data expressed as Number (%)

Table (4): demographic data within the studied groups according to age related macular degeneration staging

Variable	Group 1 Drusens only(N= 103)	Group 2 Wet Type (N= 68)	Group 3 Geographic atrophy (N= 22)	Test of sig.
Age (years)	66.61±8.77	69.01±9.70	69.18±9.65	F= 1.695 P = 0.186
Sex				
Males	22 (21.4%)	28 (41.2%)	16 (72.7%)	$\chi2$ = 23.580 P < 0.001*
Females	81 (78.6%)	40 (58.8%)	6 (27.3%)	

$\chi2$=Chi-square test MC: Monte-Carlo test F= One-way ANOVA *: Statistically significant (p< 0.05)

Table (5): clinical history and risk factors among the studied groups according to age related macular degeneration staging

Variable	Group 1 Drusens only(N= 103)	Group 2 Wet Type (N= 68)	Group 3 Geographic atrophy (N= 22)	Test of sig.
DM	59 (57.3%)	36 (52.9%)	6 (27.3%)	$\chi2 = 6.560$ P = 0.038*
HTN	90 (87.4%)	61 (89.7%)	21 (95.5%)	$\chi2 = 1.257$ P = 0.534
Hyperlipidemia	51 (49.5%)	26 (38.2%)	4 (18.2%)	MC = 7.908 P = 0.019*
Smoking	23 (22.3%)	25 (36.8%)	15 (68.2%)	$\chi2 = 18.145$ P < 0.001*
Prolonged exposure to sun	54 (52.4%)	44 (64.7%)	18 (81.8%)	$\chi2 = 7.458$ P = 0.024*

Table (6): ocular examination of the studied groups according to age related macular degeneration staging

Variable	Group 1 Drusens only(N= 103)	Group 2 Wet Type (N= 68)	Group 3 Geographic atrophy (N= 22)	Test of sig.
Previous ocular surgery	18 (17.5%)	12 (17.6%)	3 (13.6%)	MC = 0.211 P = 0.900
Normal refraction	12 (11.7%)	12 (17.6%)	12 (54.5%)	MC = 28.688 P < 0.001*
Myopia	10 (9.7%)	9 (13.2%)	5 (22.7%)	
Hypermetropia	81 (78.6%)	47 (69.1%)	5 (22.7%)	
BCVA (LogMAR)	**0.48 (0.18-1.78)**	**1.19 (0.18-1.78)**	**1.3 (0.48-1.78)**	**KW = 109.919**

MC: Monte-Carlo test $\chi2$=Chi-square test *: Statistically significant ($p< 0.05$) KW= Kruskal Wallis test

DISCUSSION

Age-related macular degeneration (AMD) is considered one of the most common leading causes of severe visual loss and blindness among people over the age of 50 years[16]. This study was carried out on patients attending Mansoura University Ophthalmic Center. In current study; age related macular degeneration had been classified into three groups: Group I: 103 eyes of 53 patients (53.4%) had drusen. Group II: 68 eyes of 58 patients (35.2%) had wet type. Group III: 22 eyes of 17 patients (11.4%) had geographic atrophy.

Previous population-based epidemiological studies, mostly involving a single race or ethnicity, have provided estimates of the prevalence and incidence of age-related macular degeneration in whites, blacks and other racial groups, with significant variability reported and confirmed in a meta-analysis[17]. The highest prevalence of any age-related macular degeneration occurred in individuals aged 75 to 84 years old,

varying from 7.4% in blacks to15.8% in whites and Chinese Americans. Similar variation in prevalence of age-related macular degeneration for whites, blacks, and Mexican Americans was reported in a National Health and Nutrition Examination Survey study[17].

In the present study; mean age of patients was 67.7 ± 9.32 with a median 68 years, 69.01±9.706 for group I, 66.61±8.77 for group II, and 69.18±9.65 for group III. This is in agreement with Al-Zamil & Yassin, 2017 study which reported that the risk of acquiring AMD increases more than three folds in patients older than 75 years compared to patients between 65 and 74 years[18].

In this study we had 193 eyes of 105 patients with age related macular degeneration, females (66.7%) were statistically significant more than males (33.3%). This is agreed with most studies of AMD which reported that females are more exposed to develop AMD more than males[10].

Sunlight exposure is thought to result in more oxidative stress in the retina, causing the development of AMD[19]. This agreed with our study as we had 59% of patients giving history of prolonged exposure to sun and this is considered statistically significant (p value =0.024).

In this study there was statistically significance between AMD and smoking (p value < 0.001), hyperlipidemia (p value =0.019), and DM (p value =0.038).

Smoking is the most consistently reported modifiable risk factor for AMD and is associated with a 2–4 folds increased risk for any form of AMD[17]. Hyperlipidemia is mostly associated with AMD than other systemic diseases as in Joachim et al., 2014 study[18].

In Saunier et al., 2018 study there were positive correlations between diabetes mellitus and the development of AMD[13].

Joachim et al., 2014 suggested that high blood pressure is associated with lower choroidal blood flow and disturbed vascular homeostasis, and this may be an explanation why we had about 90% of our studied AMD cases had hypertension[12].

In our study; there was no statistically significance between previous cataract extraction and AMD (p value = 0.900). In our study; 18.1% patients had previous ocular surgery (cataract extraction), while several large epidemiological studies have found an increased association between the development of cataract, cataract surgery and late AMD (both GA and nAMD)[19], this disagreement may be due to small number of cases showed in this study.

Regarding refraction; there was statistically significant positive correlation between AMD and hypermetropia (p value < 0.001) in agreement with Li et al., 2014, which reported that hypermetropia is associated with higher risk of AMD[19].

In current study there was statistically significant difference of BCVA among studied group (p value < 0.001), the patients with Drusen had BCVA of median 0.48 Log MAR, the patients with wet type AMD had BCVA of median 1.19 Log MAR, and the patients with geographic atrophy had BCVA of median 1.3 Log MAR. This agreed with other studies which revealed that visual affection and central visual loss is more likely with geographic atrophy and disciform scars, then in neovascular AMD, and vision is less affected in cases with drusen[20].

In this study; some preventable risk factors for AMD were detected like smoking, prolonged sun exposure, and hyperlipidemia. AMD was common in cases with DM, and HTN.

CONCLUSION

Age is the major risk factor for development and progression of AMD, females are more vulnerable to develop AMD more than males. In this study; some preventable risk factors for AMD were detected like smoking, prolonged sun exposure, and hyperlipidemia. AMD was common in cases with DM, and HTN. The most common disease among studied group was hypertension, followed by diabetes mellitus, and then hyperlipidemia. In current study; there was no significant correlation between previous cataract extraction and AMD. Regarding refraction; there was statistically significant positive correlation between AMD and hypermetropia. Visual affection and central visual loss is more likely with geographic atrophy, then in wet AMD, and vision is less affected in cases with drusen.

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Data Availability: The authors declare that all data supporting the findings of this study are available within the article and its supplementary information file.

Competing interests: The authors declare no competing interests.

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Ethics declarations: All procedures performed in the study followed the 1964 Helsinki declaration and its later amendments, University Ethics Committee approved the project.

Conflict of interest

Hanem M. Kishk, Hossam Abouelkheir, Rania Kamel, Mohamed A. Mouftah. All authors have no conflicts of interest that are directly relevant to the content of this review.

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