

Epidemiological profile of age-related macular degeneration patients in Federal University of Parana, Brazil

Perfil epidemiológico da degeneração macular relacionada à idade na Universidade Federal do Paraná, Brasil

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ABSTRACT

Objective: To evaluate the profile and severity of age-related macular degeneration (AMD) in ophthalmology ambulatory of Federal University of Parana in Curitiba, Parana, Brazil. **Methods:** This was a cross-sectional study with data collected among the 6155 outpatients ophthalmic appointments (november 2011 to november 2013). In this 6155 patients, a total of 346 patients had retinal diseases and were screened by two retinal specialists for signs of AMD. If present, they were submitted to a protocol including a new ophthalmic evaluation comprising visual acuity, tonometry, biomicroscopy, dilated fundus examination and optical coherence tomography (OCT). **Results:** A total of 6155 patients underwent ophthalmologic evaluation for several reasons. Three hundred and forty six patients had retinal diseases (incidence of 5.6%) and 68 of these (incidence of 19.6% in retinal patients) had AMD. The mean age of all patients was 53 years and in retinal patients was 60 years. In AMD patients mean age was 73 years. Ethnicity, body-mass index (BMI) and smoking habits were evaluated in the 68 patients diagnosed with AMD (34 exudative and 34 non-exudative) but none of those parameters were statistically significant comparing exudative and non-exudative forms. **Conclusion:** Most of the patients were European descendants. A higher proportion of advanced cases of AMD comparing with literature was found (50% of exudative form). Regarding ethnicity, iris color, smoking habit and BMI, there was no difference comparing exudative and non-exudative forms. These results may be compared to available AMD studies, since there is little information about AMD in Brazil.

Keywords: Macular degeneration/epidemiology; Choroidal neovascularization; Retinal drusen; Geographic atrophy

RESUMO

Objetivo: Avaliar o perfil epidemiológico e severidade da degeneração macular relacionada à idade (DMRI) no ambulatório de oftalmologia da Universidade Federal do Paraná (UFPR) em Curitiba, Paraná, Brasil. **Métodos:** Estudo transversal com dados coletados referentes as 6155 consultas oftalmológicas realizadas no período de novembro de 2011 a novembro de 2013. Destes, 346 pacientes possuíam doenças retinianas e foram avaliados por dois especialistas em retina à procura de sinais de DMRI. Os confirmados foram submetidos a um protocolo compreendendo acuidade visual, tonometria, biomicroscopia, oftalmoscopia indireta sob midríase e tomografia de coerência óptica (OCT). **Resultados:** Um total de 6155 pacientes foram submetidos à consulta oftalmológica na UFPR. Trezentos e quarenta e seis pacientes apresentaram doenças retinianas (incidência de 5.6%) e 68 destes (incidência de 19.6% dos pacientes com doenças de retina) apresentaram DMRI. A média de idade dos pacientes do ambulatório geral foi de 53 anos e em pacientes com doenças de retina foi de 60 anos. Pacientes com DMRI tinham em média 73 anos. Etnia, cor da íris, índice de massa corpórea (IMC) e tabagismo foram avaliados nos 68 pacientes diagnosticados com DMRI (34 exsudativa e 34 não exsudativa), mas nenhum dos parâmetros foram estatisticamente significantes. **Conclusão:** A maioria dos pacientes eram de origem europeia. Comparando com a literatura, uma maior proporção de casos avançados de DMRI (50% de forma exsudativa) foi encontrada. Em relação à etnia, tabagismo e IMC, não houve diferença entre pacientes com forma exsudativa e não exsudativa. Estes resultados podem ser comparados com estudos disponíveis, considerando a pouca informação referente a DMRI existente no Brasil.

Descritores: Degeneração macular/epidemiologia; Neovascularização de coróide; Drusas retinianas; Atrofia geográfica

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INTRODUCTION

Age-related macular degeneration (AMD) is a multifactorial disease, with an increasing prevalence worldwide and significant morbidity. The first studies, in the early 1980s, pointed to the significant burden that AMD would represent in the years to come. The AMD is the leading cause of legal blindness in the Western world in people over 50 years old.⁽¹⁾ Only in United States (US), 9.2% of the population over 40 years have signs of AMD⁽²⁾. In France, AMD is the leading cause of blindness in population over 50 years, with a prevalence of 8.50% and increasing with age reaching up to 27.9% in people over 75 years^(3,4). It decreases the reading and driving abilities, as well as all activities that need an accurate sight^(5,6). It is expected a 50% increase in number of individuals affected by AMD until 2020⁽⁷⁾.

There is no official epidemiologic statistic of AMD in Brazil but some studies suggest numbers⁽⁸⁾. In a recent global meta-analysis including 149 studies, only 39 used international protocols of screening and imaging and were considered reliable. In this meta-analysis, only one was from Latin America⁽⁹⁾. This study, held in Londrina, Brazil, indicate a prevalence of 15.1% of AMD in that population over 60 years. Another study held Veranópolis, Brazil, showed an AMD prevalence of 30.5% in patients above 80 years, but was not included in global data due to its methodology⁽⁹⁾. It is important to note that both Brazilian studies collected data from specific groups (eastern descent or older than 80 years)^(10,11). The Brazilian Institute of Geography and Statistics estimated approximately 285 thousand inhabitants over 55 years old in Curitiba, Paraná, Brazil in 2013⁽¹²⁾. Applying an estimated AMD prevalence of 6 to 10% (Europe and US), it is expected around 17 to 28 thousand cases – all forms of AMD – in Curitiba, Brazil.

Age is the major risk factor for AMD. Studies indicate an oxidative damage of retinal pigmented epithelium (RPE) and choriocapillaris, including a decrease in plasmatic levels of glutathione, C and E vitamins and catalase activity. An increase in lipofuscin levels in RPE was observed too^(13,14). However a variety of factors are involved in its pathogenesis. The hereditary polygenic component is among the main risk factors for developing the disease^(15,16), and a variety of other factors are involved, including ethnicity, genetics^(17,18), family history, exposure to UVB rays, vitamins deficiency⁽¹⁹⁾, high body mass index (BMI; range 25 to 30 – overweight and > 30 – obese) and smoking.⁽²⁰⁾

In this study we tried to assess the epidemiological profile of AMD and the presence of known risk factors in AMD cases, such as age, obesity, ethnicity and smoking habits.

METHODS

This is a cross-sectional study conducted according to the Declaration of Helsinki. All patients were submitted to a written informed consent and examined by two retina specialists in vision center at the Federal University of Paraná. The study was approved by ethics committee of Clinical Hospital, Federal University of Parana, in Curitiba, Brazil.

Patients were recruited from november 2011 to november 2013, during the regularly scheduled ophthalmologic evaluation at the “Vision Center” - Department of Ophthalmology - Federal University of Paraná in Curitiba; Brazil. Patients with any retinal suspicious characteristics were evaluated by two retina specialists and were included in the study only if met the following criteria:

- Age above 55 years;
- History of AMD presenting large confluent soft drusen

(>125 μm) in both eyes or one eye with large drusen and fellow eye with either geographic atrophy (> 360 μm) or signs of choroidal neovascularization;

- No eye disease other than previous cataract uncomplicated extraction;
- No history of diabetes or uncontrolled systemic arterial hypertension (self reported use of medication or physician diagnosed);
- No signs of degenerative myopia (refractive error greater than -4.00 diopters with signs of retinal degenerations such as lacquer cracks, posterior staphyloma, tilted optic disc, retinoschisis etc).

All patients underwent a complete ophthalmologic examination including a best corrected visual acuity test using an ETDRS “model 2” chartTM (Good-Lite, Elgin, IL) without mydriasis, biomicroscopy using a Topcon SL-1ETM slit lamp (Topcon, Oakland, NJ), Goldmann tonometry and a fundus exam after mydriasis with tropicamide, performed by a retina specialist using a Heine EN30TM indirect ophthalmoscope (Heine, Kientalstraße 7, Herrsching) and a VolkTM 20 diopters lens (Volk, Mentor, OH). Patients who met the study criteria were submitted to an optical coherence tomography (OCT) image from both eyes with specific image protocol using a Zeiss Stratus OCTTM (software version 4.0.2, Macular Normative Data Feature MAC-3244 – Carl Zeiss Meditec, Göschwitzer Straße, Jena).

Additional fluorescein angiogram was performed in some patients in whom there was any diagnostic doubt (vascular diseases, macular dystrophies, etc.) using a Topcon TRC50xTM (Topcon, Oakland, NJ), with intravenous 20% sodium fluorescein (Oft vision, Tatuapé, São Paulo).

Finally, the AMD patients were classified as non-exudative (“dry”) if macular drusen with at least 62 μm were found. If signs of choroidal neovascularization (active bleeding or history of previous intravitreal therapy, etc.) were found, they were included as exudative (“wet” form).

Imaging Protocol

In order to ensure that AMD patients had the specified criteria and no other macular disease, an OCT image was performed for each patient, using a protocol according to “*University of Wisconsin – School of Medicine and Public Health – Fundus Photograph Reading Center – Non-study Specific Stratus Optical Coherence Tomography (OCT 3)*”. Two scan types were performed: the Fast Macular Thickness Map scan and the Cross Hair scan. All subjects had one Fast Macular Thickness Map (centered on macula, the retinal boundaries indicated by white lines on the underlying scans (the internal limiting membrane and the retinal pigment epithelium) did not contain obvious major errors at the center of the macula) and a 6mm Cross Hair scan centered on foveal region. A minimal signal strength of 5 was necessary.

Statistical analysis

Estimated cases of AMD in Curitiba (city in south region of Brazil) using demographic features of Brazilian census in 2014. In order to set de confidence interval found, an online calculator was used⁽²¹⁾. For data analysis, Prism 6.0cTM (GraphPad Software, La Jolla, CA, USA 2013) was used, t-test, Fisher exact test, One-way ANOVA (Analysis of Variance) Tukey’s post hoc or Qui-square test used to single and demographics comparisons (age, ethnicity, gender, smoking habit and BMI). Values under 5% were considered significant.

A total of 6155 patients underwent ophthalmologic examination from november 2011 to november 2013 in vision center at Federal University of Parana. Three hundred and forty six of them had suspected retinal diseases and were evaluated

by two retina specialists. Any suspected case of AMD was submitted to the protocol already described.

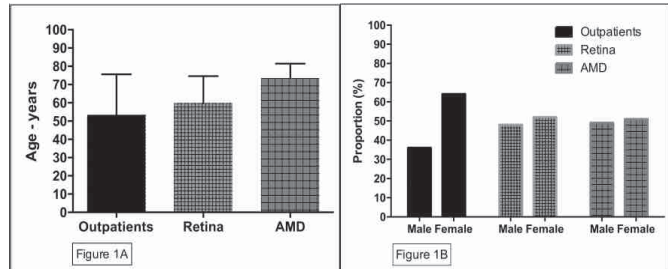
RESULTS

In these 2 years, a total of 68 patients with AMD and no other conditions that could somehow interfere in diagnosis and staging – such as diabetes – were included. The mean age of outpatients group was 53 years (SD±22; range 0 -102 years). In the retina group was 60 years (SD±15; range 0-88 years) and AMD group was 73 years (SD±8.2; range 55-88 years). If these groups are compared, there was a significant difference in mean age among them. Comparing outpatients, retina patients and AMD with each other, a significant difference was found (p<0.001, ANOVA). Furthermore, there was a larger number of female patients in all groups. In outpatients, 3941 (64%) were female, while in retina was 181 (52%) and AMD was 35 (51%) Table 1 and Figures 1A and 1B.

Table 1
Demographic data from outpatients, retina and AMD

Variables	Outpatients (n = 346)	Retina (n = 6155)	AMD (n = 68)	P value
Age (±SD) years	53 ±22	60 ±15	73 ±8.2	p < 0.001*
Gender				
Male	2216 (36%)	165 (48%)	33 (49%)	p = 0.12**
Female	3941 (64%)	181 (52%)	35 (51%)	

(*)One-way ANOVA with Tukey ad hoc; (**)Chi-square test



Figures 1A: Age average and standard deviation; and **1B.** Gender proportions in groups

The AMD group included 68 subjects (63 European descendants and 5 Afro-descendants, 33 men and 35 women), being 34 with exudative form and 34 with non-exudative. There was no significant difference for age, gender or BMI among the groups. Regarding the age, comparing both groups, a mean of 73 years (SD±7.7; range 55-88 years) was found in non-exudative AMD and a mean of 73 years (SD±8.8; range 55-88 years) in exudative. A slightly predominance of females in non-exudative AMD (53%) and an equal number in exudative (50%). A larger number of European descendants in both non-exudative (91%) and exudative (94%) was observed, without difference in groups however. Regarding the iris color, a higher number of patients with a light iris (either blue or green) was found in the exudative group comparing to the non-exudative (p = 0.0506). A well known risk factor for AMD, smoking habit, was not different in AMD groups. Nevertheless, a higher percentage of smokers in exudative against non-exudative group (44% vs. 29%) was found. Finally, the overweight patients outscored the normal weight patients in both groups; 53% in non-exudative and 56% in exudative; but no difference comparing groups was observed, as shown on table 2.

Table 2
Demographic data from AMD patients and controls

	AMD non-exudative (n = 34)	AMD exudative (n = 34)	P-value
Age (±SD) years	73 ±7.70	73 ±8.80	p = 0.88*
Gender			
Male	16 (47%)	17 (50%)	p = 1.00**
Female	17 (50%)	18 (53%)	
Ethnicity			
European descendants	31 (91%)	32 (94%)	p = 1.00**
Afro descendants	5 (9%)	2 (6%)	
Iris color***			
Dark	23 (68%)	14 (41%)	p = 0.05**
Light	20 (59%)	11 (32%)	
Smoking****			
Yes	10 (29%)	15 (44%)	p = 0.31**
No	24 (71%)	19 (56%)	
BMI			
Normal	16 (47%)	15 (44%)	p = 1.00**
Pre-obesity and obesity	18 (53%)	19 (56%)	

AMD: age macular degeneration; BMI: body mass index; (*) t-test; (**) Fisher’s exact test; (***)Light (blue or green); Dark (all the others) (****) One or more pack-year

DISCUSSION

The incidence and prevalence of AMD is increasing in different populations, including Brazil. Until now, its exact pathophysiology remains unknown but environment and genetics factors, as in most of diseases, must both be present. Factors such as increased life expectancy, sun exposure, smoking, obesity, inflammation among others contribute to AMD development^(6,7,22). Currently, AMD is the leading cause of vision loss in industrialized countries^(2,9). The Brazil’s south region population has, mostly, an European ancestry (not forgetting the high miscegenation in Brazilian population). It is well known that ethnicity has a major role in AMD development. The solar exposure, presumably due to ultraviolet rays, may interfere in AMD development. A similar prevalence of European inhabitants could be inferred for the Brazil’s south region and (around 8 to 27%) and similar to central America in north region^(4,9,23–27).

A mean age of 73 years for AMD patients was found. This is in agreement the expected age, since an increment in cases usually occurs after 65 years⁽⁹⁾.

According to the literature, a proportion of about 10% of exudative AMD would be expected⁽²⁸⁾. Even so, 50% of patients had exudative form. We assume some reasons: a public tertiary hospital, where only the most severe cases were being sent. A delay or some difficulty in scheduling an ophthalmologic appointment. Also the high cost of treatment for exudative AMD could force patients to seek for public service.

The results of this study may be compared to available studies of AMD. A higher incidence of exudative and late AMD compared to the literature may be explained by the strict protocol collection at a reference center. In Brazil, insufficient data about AMD and the little knowledge of population and health

professionals about it, makes it a great challenge to know the real incidence. We believe that reliable data could guide public policies of early diagnosis and treatment, resulting a lower morbidity with better financial and social cost outcomes⁽²⁹⁻³³⁾.

Age-related macular degeneration is serious sight-threatening disease. Nevertheless, there is little information about the real impact of it in Brazil, even in major ophthalmology services. We hope that these data can help to facilitate the access of AMD early disease cases as well, preserving the patients sight and quality of life.

CONCLUSION

Most of the patients were European descendants. A higher proportion of advanced cases of AMD comparing with literature were found (50% of exudative form). Regarding ethnicity, smoking habit and BMI, there was no difference comparing exudative and non-exudative forms. These results may be compared to available AMD studies, since there is little information about AMD in Brazil.

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