Polskie Towarzystwo Okulistyczne
www.pto.com.pl

KLINIKA OCZNA 2023, 125, 3: 158-162
Received: 6.04.2022 Accepted: 8.08.2022

ORIGINAL ARTICLE

Access this article online

Website:
www.klinikaoczna.pl

DOI:
https://doi.org/10.5114/ko.2023.131907

Assessment of age-related macular degeneration (AMD) risk factors in AMD patients and healthy people over 40 years old in the Polish population

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ABSTRACT

Aim of the study: To assess the prevalence of age-related macular degeneration (AMD) risk factors in the Polish population of AMD patients and healthy individuals over 40 years of age.

Material and methods: The Simplified Thea AMD Risk-Assessment Scale (STARS) was performed on people aged over 40 years old including AMD patients in Poland. The questionnaire contained questions about demographics and AMD risk factors.

Results: Data were obtained from 233 adults (65% were female). 54% of participants were in the age range of 40-64, 23% in the range 65-74 and 23% in the 75+ group. Age-related macular degeneration was reported in 90 cases, more often in adults over 65 years old ($p < 0.001$). Patients with AMD were more frequently diagnosed with hypertension ($p = 0.006$), hypercholesterolemia ($p = 0.002$) and arteriosclerosis ($p = 0.03$) compared to adults without AMD. Phacoemulsification procedures had been performed more often in the AMD group compared to the healthy one ($p < 0.001$). Smoking was more common in people with AMD ($p = 0.004$). STARS median score in the overall group was 9.5 points (0-30). The score was significantly higher in the AMD group compared with the no AMD group ($p < 0.001$). The distribution between low, moderate and high risk groups was respectively 32%, 60% and 13% in the AMD group, and 75%, 24% and 1% in the healthy group; the difference was statistically significant ($p < 0.001$).

Conclusions: Most AMD risk factors included in the questionnaire occurred more often in AMD patients. Therefore, it could be useful in determining the high risk of AMD in the Polish population. Moreover, there is a need for wider education about healthy lifestyle which influences AMD risk.

KEY WORDS: risk factors, epidemiology, age-related macular degeneration, Polish population.

INTRODUCTION

The main cause of blindness in Western populations is age-related macular degeneration (AMD) [1]. It is also the most prevalent retinal disease in this part of the world [2]. Globally, the number of AMD patients is predicted to increase from approximately 196 million in 2020 to 288 million in 2040 [3]. Recently, major improvement has been made in the comprehension as well as the treatment of this eye condition. Especially, intravitreal injections of antiangiogenic agents make it possible to stabilize or even reverse progression of neovascular AMD. However, early diagnosis is crucial for their efficacy [4]. As a consequence, there is a need for a test which will enable doctors to determine high risk populations, observe them and start treatment as soon as possible. Therefore, the aim of our study was to assess the prevalence of AMD risk factors in the Polish population of AMD patients and healthy individuals over 40 years of age. Thus, after analyzing articles on that topic, the decision to use the Simplified Thea AMD Risk-Assessment Scale (STARS) questionnaire was made. STARS is simple, short, translated into Polish and self-administered [5].

MATERIAL AND METHODS

The STARS questionnaire was performed on people aged over 40 years old including self-reported AMD patients in the outpatient clinics in University Clinical Center Prof. Kornel Gibiński of the Medical University of Silesia in Katowice and in Provincial Specialist Hospital Blessed Virgin Mary in Czestochowa as well as through an online survey posted on social media with a short invitation. The questionnaire con-

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tained 14 questions about demographics and AMD risk factors stated in STARS – Figure 1A (in Polish) and Figure 1B (in English). We provided every interviewee with the opportunity to learn their STARS score with details on which modifiable factors influenced the result. The data were collected from October 2019 to October 2020 and analyzed anonymously in the program Statistica 13.3. A total of 233 questionnaires were obtained. Statistical analyses included

A

Skala oceny ryzyka zachorowania na AMD (zwyrodnienie plamki żółtej związanej z wiekiem) u osób powyżej 40. roku życia

Jako członkowie SKN przy Klinice Okulistyki ŚUM w Katowicach chcielibyśmy przeprowadzić z Państwem ankietę dotyczącą stopnia ryzyka wystąpienia u Państwa AMD. Ankieta posłuży badaniom naukowym. Udział w ankiecie jest dobrowolny i nie wymaga podania danych osobowych.

1. Ile ma Pani/Pan lat?
   ☐ 40-64
   ☐ 65-74
   ☐ > 74
2. Jaka jest Pani/Pana płeć?
   ☐ Kobieta
   ☐ Mężczyzna
3. Czy choruje Pani/Pan na AMD (zwyrodnienie plamki żółtej związanej z wiekiem)?
   ☐ Tak
   ☐ Nie
4. Czy rodzice chorują bądź rodzeństwo choruje na AMD (zwyrodnienie plamki związane z wiekiem)?
   ☐ Tak
   ☐ Nie
5. Ile Pani/Pan waży (w kilogramach)? _____
6. Ile ma Pani/Pan wzrostu (w centymetrach)? _____
7. Czy pali/ paliła/palił Pani/ Pan papierosy (tradycyjne lub elektroniczne)?
   ☐ Obecnie
   ☐ W przeszłości (zaprzestanie palenia mniej niż 10 lat temu)
   ☐ W przeszłości (zaprzestanie palenia ponad 10 lat temu)
   ☐ Nigdy nie paliłam/paliłem
8. Czy była/był Pani/Pan narażona/narażony na bierne palenie tytoniu w domu/pracy?
   ☐ Tak
   ☐ Nie
9. Czy ma Pani/Pan stwierdzone nadciśnienie tętnicze?
   ☐ Tak
   ☐ Nie
10. Czy przebyła/przebył Pani/Pan zawał serca?
    ☐ Tak
    ☐ Nie
11. Czy ma/miała/miał Pani/Pan stwierdzoną hipercholesterolemię (zbyt wysoki poziom cholesterolu)?
    ☐ Tak
    ☐ Nie
12. Czy stwierdzono u Pani/Pana miażdżycę?
    ☐ Tak
    ☐ Nie
13. Czy przeszła/przeszedł Pani/Pan operację zaćmy?
    ☐ Tak
    ☐ Nie
14. Czy występują u Pani/Pana wady refrakcji?
    ☐ Krótkowzroczność
    ☐ Nadwzroczność
    ☐ Nie występują

Dziękujemy za wypełnienie ankiety. Jeśli jest Pani/Pan zainteresowana/y wynikiem ryzyka zachorowania na AMD, prosimy o podanie adresu mailowego, na który zostanie przesłanie podsumowanie kwestionariusza.

_____

B

AMD (age-related macular degeneration) Risk Assessment Scale in individuals over 40 years old

As members of Students' Scientific Society, the Department of Ophthalmology, Faculty of Medical Sciences, Medical University of Silesia in Katowice, we would like to conduct a survey with you regarding the risk of AMD. The results will be used in scientific research. Participation in the survey is voluntary and does not require providing personal data.

1. How old are you?
   ☐ 40-64
   ☐ 65-74
   ☐ > 74
2. What is your sex?
   ☐ Female
   ☐ Male
3. Do you have AMD (age-related macular degeneration)?
   ☐ Yes
   ☐ No
4. Do your parents or siblings have AMD (age-related macular degeneration)?
   ☐ Yes
   ☐ No
5. How much do you weigh (in kilograms)? _____
6. How tall are you (in centimeters)? _____
7. Do you smoke/ have you smoked cigarettes (traditional or electronic)?
   ☐ I currently smoke
   ☐ I am a former smoker (I quit less than 10 years ago)
   ☐ I am a former smoker (I quit more than 10 years ago)
   ☐ I have never smoked
8. Have you been exposed to passive smoking at home or at work?
   ☐ Yes
   ☐ No
9. Are you diagnosed with arterial hypertension?
   ☐ Yes
   ☐ No
10. Have you ever had a heart attack?
    ☐ Yes
    ☐ No
11. Are you diagnosed with hypercholesterolemia (too high cholesterol levels)?
    ☐ Yes
    ☐ No
12. Are you diagnosed with arteriosclerosis?
    ☐ Yes
    ☐ No
13. Have you undergone a cataract surgery?
    ☐ Yes
    ☐ No
14. Do you have any refractive errors?
    ☐ Myopia
    ☐ Hyperopia
    ☐ None

Thank you for completing this survey. If you are interested in the result of AMD risk scale, please provide your email address to which the questionnaire's summary will be sent.

_____

Figure 1. A) The questionnaire used in the study; **B**) the questionnaire used in the study (translated into English)

descriptive methods as well as association and significance of difference methods. Chi-square tests were performed for the categorical data. When class size was less than five, the exact Fisher's test was used. For quantitative data the Shapiro-Wilk test was used to assess data distribution normality. We applied Mann-Whitney U-test test to compare the differences among the groups because they were found to be non-normally distributed. A p-value of 0.05 was considered statistically significant.

RESULTS

Data were obtained from 233 adults. Of these 65% were female (F). Women accounted for 61% of patients and 67% of the healthy group ($p = 0.35$). 54% of people were in the age range 40 to 64, 23% in the range 65 to 74 and 23% were over 74 years old. Ninety cases of AMD were reported. AMD was observed more often in adults over 65 years old ($p < 0.001$). All respondents were of Caucasian descent. Self-reported AMD family history prevalence was 10%, 11% in AMD patients and 9% in people without this disease ($p = 0.6$).

Mean body mass index (BMI) was 26. It did not differ significantly between the groups ($p = 0.07$). Sixty percent of participants had abnormal BMI indicating overweight (AMD: 52%, healthy: 39%) or obesity (AMD: 16%, healthy: 16%). One percent of participants in both groups were underweight.

Current, former ≤10 years, former >10 years and never smokers made up respectively 16%, 9%, 39% and 37% of the AMD group and 11%, 8%, 20% and 61% of the no AMD group ($p = 0.009$). Smoking was more common in people with AMD ($p = 0.004$).

AMD patients were more often diagnosed with hypertension ($p < 0.001$) compared to adults without AMD. People reported myocardial infarction in 9% in the AMD and 3% in the healthy group but the difference was not statistically significant ($p = 0.08$). Also, hypercholesterolemia ($p < 0.001$) and arteriosclerosis ($p < 0.001$) were correlated with AMD.

Phacoemulsification procedures had been performed more often in the AMD patients compared to the other group ($p < 0.001$). However, it was apparent in the 40-64 years of age group ($p < 0.001$) but not in the older age groups ($p > 0.05$).

There were no statistical differences in occurrence of myopia, hyperopia and no refractive errors between the groups ($p > 0.05$).

STARS median score in the overall group was 9.5 points (0-30). Median score in the AMD group was 14 points and in the no AMD group 5 points ($p < 0.001$). The distribution between low, moderate and high risk groups was respectively 32%, 60% and 13% in the AMD group, 75%, 24% and 1% in the no AMD; and the difference was statistically significant ($p < 0.001$).

DISCUSSION

To our knowledge, this is the first published study on STARS or different questionnaires related to AMD risk factors used in the Polish population. Other recent studies which involved Polish AMD patients concerned analysis of antioxidative enzymes related to AMD risk development. A significant decrease in those enzymes might lead to damage of photoreceptors and retinal pigment epithelium cells and had an important role in AMD progression [6].

The selection as well as the score of each risk factor included in STARS derived from research conducted on approximately twelve thousand Italian patients and validated on a population of over six thousand French [5].

The epidemiological data have been inconsistent regarding the sex-specific risk of AMD. Sex was not significantly associated with AMD in our study. Many studies including meta-analysis [7] have produced similar results to ours in terms of the correlation between sex and AMD [8, 9]. On the other hand GlobalData epidemiologists found that 65.76% of diagnosed incident cases of AMD occurred in women while men accounted for 34.24% in the seven major pharmaceutical markets [10]. An explanation for this phenomenon could be the longer life expectancy of women compared to men, which makes them more likely to acquire age-dependent diseases. However, in this Korean cross-sectional study male population was at a greater risk for late-AMD [11]. AMD prevalence rose with the increasing age of the respondents and it was observed more often in adults over 65 years old in our research. Those findings were confirmed by Weih *et al.* [12] and Klaver *et al.* [13].

We did not deeply examine race as a risk factor of AMD because all our respondents were Caucasian. Nevertheless, earlier research – by Lazreg *et al.* [14] indicated that North-African ethnicity was associated with this disease.

In contrast to a previously cited article by Chakravarthy *et al.* [7], in our study self-reported AMD family history was similar in AMD and no AMD groups despite being one of the risk factors. The possible explanation is that healthy respondents with family members with AMD could have been more interested in our research than people who have never heard about it.

In our study, the difference in the presence of AMD between the BMI groups – underweight, healthy, overweight, obese was not significant. However, the majority – 60% of our respondents were overweight and according to other research – by Clemons *et al.* [15] the association with AMD was only made with obese patients. Furthermore, physical activity tended to decrease the risk of AMD progressing – Seddon *et al.* [16]. Therefore, obesity was considered as the modifiable AMD risk factor and losing weight was also recommended.

Chakravarthy *et al.* [7] and Joachim *et al.* [17] classified smoking cigarettes currently and in the past as risk factors of AMD. Those findings were proved in the combined analysis based on three similar populations from North America, Europe and Australia – Smith *et al.* [18]. Our survey supported these results but we did not analyze smoking pack-years like Clemons *et al.* [15]. Consequently, both AMD patients and people in the risk group for developing AMD were strongly advised against smoking and quitting is recommended [19].

In our study, hypertension (HT) was correlated with AMD incidence. The resembling findings were from the Age-Related Eye Disease Study Research Group [20]. AMD patients with hypertension showed decreased choroidal blood flow in comparison to those without history of HT in this study [21]. The impaired choroidal perfusion might result in insufficient elimination of degradation products from retinal pigment epithelium and the formation of drusen. Reduced blood flow contributes to hypoxia and promotes vascular endothelial growth factor (VEGF) upregulation and neovascularization [22]. Accordingly the prevention of hypertension should be considered as an important public health issue. Additionally, the presence of HT is contemplated to reduce the potential for functional improvement caused by the application of anti-VEGF therapy in neovascular AMD [23-25] though some studies did not find that correlation [26, 27]. Further research is needed to evaluate the impact of methods of HT treatment on visual outcomes of AMD patients.

Myocardial infarction was more common in the AMD group but the result was not statistically significant probably because of the small group size. Similar results involving cardiovascular diseases were obtained by Chakravarthy *et al.* [7].

Increased level of total serum cholesterol was correlated with AMD incidence. Similarly to previous research – by Tan *et al*. [28] and Tomany *et al.* [29]. That relationship was not readily explained. Arteriosclerosis was correlated with AMD incidence. There were no clear results in the literature about that topic. However, arteriosclerosis is obviously connected to hypercholesterolemia.

Phacoemulsification was more common in AMD patients but only in the 40-64 age group. The findings from epidemiological studies regarding these associations have been inconsistent. Studies by Chakravarthy *et al.* [7] and Freeman *et al.* [30] supported this association. It could reflect shared risk factors and the fact that both are diseases that affect the aging eye, there is concern that surgery may predispose the operated eye to the development of neovascular AMD. However, there are pooled reports which do not support this association [31]. These results also showed no clear effect of cataract surgery on the risk of progression to advanced AMD [31].

Despite the fact that in our study there were no significant differences in occurrence of myopia, hyperopia and no refractive errors between the groups, there was research which found that refractive error, especially hyperopia, was correlated with AMD [32]. Several possible explanations have been proposed over the past few decades. Hyperopic eyes are believed to have increased scleral rigidity, which leads to impairment of the choroidal blood flow in the eyes with shorter axial length [33, 34]. It is possible that decreased flow contributes to the neovascularization, drusen formation, poorer thermoregulation and higher susceptibility to oxidative stress [33, 34]. There could be genetic link between hyperopia and AMD. In this Korean study there was a statistically significant negative correlation of myopia with any AMD in the female group [35]. Myopic eyes are known to have a less rigid sclera compared to hyperopic eyes [34]. Decreased concentration of VEGF in myopic eyes can cause decreased angiogenesis [36]. A further possible explanation is the use of spectacles by myopic patients resulting in reduced exposure to ultraviolet rays from sunlight, a risk factor for AMD [37].

In our study, the STARS median score was higher in the AMD group than in the no AMD group similarly to Delcourt *et al*. [5]. What is more, the difference of the distribution between low, moderate and high risk groups was statistically significant. Therefore, it could be useful in determining the high risk population of this disease in the Polish population.

Additionally, all interviewees had the possibility to find out their STARS score as well as discuss the possible ways to improve their health and reduce AMD risk or its progression.

Our study has some limitations. Data were self-reported by the participants. Therefore the presence of AMD was not verified. Group size could have played a role in the results.

CONCLUSIONS

Most AMD risk factors included in the STARS questionnaire occurred more often in AMD patients in our study. Therefore, it could be useful in determining the high risk population of this disease. Regrettably, in spite of getting a low risk score in STARS, there was still a possibility to develop this eye condition. Moreover, a wider education about healthy lifestyle which influences AMD risk is necessary. Finally, risk factors and causes of AMD require further attention and investigation.

ACKNOWLEDGMENTS

We would like to thank Dr Katarzyna Grzybek-Oleś, the ophthalmologist in Provincial Specialist Hospital Blessed Virgin Mary in Czestochowa and Prof. Ewa Mrukwa-Kominek, the Chair of the Department of Ophthalmology, Medical University of Silesia in Katowice, for the ability to collect questionnaires from AMD patients in their respective institutions.

DISCLOSURE

The authors declare no conflict of interests.

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