Review Article

Age-Related Macular Degeneration Prevalence and its Risk Factors in Iran: A Systematic Review and Meta-Analysis Study

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Abstract

Purpose: To estimate the prevalence of age-related macular degeneration (AMD) and determine its risk factors in Iran.

Methods: A comprehensive electronic search was conducted in PubMed, Scopus, Web of Science, and Google Scholar, with no restrictions on time or language of publication. Eleven studies meeting the eligibility criteria were included. Six studies with a total sample size of 9930 were included in the meta-analysis to calculate the overall prevalence of AMD in Iran. Meta-analysis was performed using Stata/MP version 15.0. Risk of bias assessment was carried out based on the Newcastle–Ottawa Scale.

Results: All participants in the studies were over 40 years old. The pooled prevalence of AMD was estimated to be 9.9% (95% confidence interval [CI]: 6.3%–13.5%). After accounting for publication bias, this estimated decreased to 6.4% (95% CI: 4%–10.2%). Smoking (odds ratio [OR]: 1.781; 95% CI: 1.152–2.756), hypertension (HTN) (OR: 1.512; 95% CI: 1.119–2.044), diabetes mellitus (DM) (OR: 1.545; 95% CI: 1.088–2.194), and hyperlipidemia (OR: 1.512; 95% CI: 1.055–2.165) were identified as AMD risk factors.

Conclusion: Based on the results of the present review, the prevalence of AMD in the Iranian population over 40 years of age is estimated to be 6.4%, and having a history of smoking, HTN, DM, and hyperlipidemia are identified as risk factors of AMD in Iran. Further original studies are needed to draw more accurate conclusions.

Keywords: Age-related macular degeneration, Iran, Prevalence, Risk factor

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Introduction

Age-related macular degeneration (AMD) is one of the main causes of irreversible blindness, gradually destroying the macula region of the retina and causing progressive central vision impairment.[1] The etiology of AMD is complex, and a combination of genetic and environmental factors is effective in its incidence.[2] As the name of this disease suggests, aging is the most important risk factor of AMD, and it usually occurs in people over 60 years of age.[1,3] In addition to aging, the impact of other environmental and nongenetic risk factors, such as smoking and diet, on the development of AMD has been indicated in previous studies.[1,3,4]

According to previous reports, AMD has a high prevalence in different regions and is the third leading cause of visual impairment and blindness in the world.[5-7] The estimates indicate that about 200 million people around the world are affected by various types of this disease, and this number is projected to reach 300 million people by 2040.[7] On the other hand, visual impairment caused by AMD has a great impact on the quality of life of patients, leading to increased stress, reduced physical activity, and higher rates of depression;[8] according to these problems, the global disability-adjusted life year caused by AMD in 2017 was estimated at 5.3

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million, representing a 108% increase compared to 1990.[9] In addition, estimates show that this disease imposes a high cost on the health-care system, so that in the United States, it has directly cost the health system 4.6 billion US dollars annually.[9] Therefore, it can be concluded that due to the relatively high prevalence of the AMD and the substantial costs, it imposes on the health-care system, it is considered one of the important public health issues. On the other hand, the prevalence of AMD and its risk factors vary in different geographical locations.[10] The purpose of this systematic review and meta-analysis was to estimate the overall prevalence of AMD in Iran and identify its main nongenetic risk factors in this country.

Methods

The present study is a systematic review and meta-analysis which is implemented according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and the MOOSE reporting guideline for meta-analysis of observational studies in epidemiology.[11,12] The study protocol has been approved by the Research and Ethics Committee of the Iran University of Medical Sciences (ID: IR.IUMS.FMD.REC.1400.020).

Search strategy and information sources

A sensitive search strategy was developed by authors and cross-checked with an expert Librarian. Combination of Medical Subject Headings and keywords including the synonyms of "Age related macular degeneration", "prevalence", "Incidence", "risk factors", "age", "smoking", "diabetes", "hyperlipidemia", "hypertension", "myopia", and "Iran" were used to develop the search sentences [the complete search sentences are available in Supplementary Tables 1-4]. On April 10, 2022, medical databases including PubMed, Scopus, Web of Science, and Google Scholar (as a cumulative database) were searched with no restrictions on time or language of publication. In addition to these databases, a search with Persian keywords was also conducted in Iranian sources including SID and Magiran to obtain more local articles that reported the prevalence of AMD in Iran.

Eligibility criteria

Primary research articles with cross-sectional, case–control, and cohort designs that reported the incidence, prevalence, or environmental risk factors of the AMD in Iran were eligible for inclusion in the present study. Furthermore, the exclusion criteria consisted of (1) primary research studies conducted in other countries or included other nationalities and (2) other types of studies including case-reports, reviews, or qualitative studies.

Study screening and data extraction

Two authors (PP and AK) independently assessed the extracted articles from the searches and imported the data using Endnote X9 (Clarivate Analytics, Philadelphia, USA). At the first step, each of them screened the articles based on the titles and abstracts and then assigned each study to the accepted or rejected groups. Then, the full text of the accepted articles was reviewed by them for executed the final inclusion process. At the end of the screening process, discrepancies between authors were resolved through conversation, and there was no need for the involvement of a third party. After these steps, data from the final selected articles were extracted by two authors independently. Extracted data contained study characteristics, number of patients with AMD (AMD prevalence was only calculated in subgroups with patients over 40 years of age), crude odds ratios (OR) for reported risk factors, and demographic variables. If the mentioned values were not directly stated in a study, they were calculated by the authors whenever possible.

Quality assessment and data analysis

Risk of bias assessment was performed by the Newcastle–Ottawa Scale (NOS) for case–control and cohort studies.[13] Furthermore, the modified version of NOS which is developed by Herzog *et al*. was used for appraising cross-sectional studies.[14] Based on this scale, each study was assigned a score, a score of 9–10 was considered very good, a score of 7–8 was considered good, a score of 5–6 was considered acceptable, and a score below 4 was considered unacceptable in this review. The studies with at least acceptable quality enrolled in the meta-analysis for estimating the AMD prevalence and determining its environmental risk factors.

Meta-analysis was done by Stata/MP version 15.0 (StataCorp LLC, College Station, Texas, USA). To indicate the effect size of the environmental factors on AMD occurrence, pooled OR was calculated and reported. Pooled OR and pooled prevalence of AMD were calculated using *metan* and *metaprop* commands, respectively. Heterogeneity between studies was assessed by the Cochran's Q-test, and degree of inconsistency (I^2) ≥50% was considered meaningful.[15,16] Whenever the heterogeneity across the studies was significant, random effect model was used to analyze pooled estimates. To explore the source of heterogeneity across the studies, meta-regression was performed using the *metareg* command. Moreover, Egger's test was used for the appraisal of publication bias, and whenever needed, *metatrim* command was used to trim and fill the studies. Finally, to evaluate the influence of each study on the final result, *metainf* was used. All outcomes of interest were calculated and reported with a 95% confidence interval (CI).

Results

Study selection and study characteristics

The electronic search strategy yielded 2310 studies, including 203 studies from PubMed, 1518 studies from Scopus, 80 studies from Web of Science, 9 studies from Persian databases, and the first 500 studies from Google Scholar search result. After removing duplicates, 1872 studies remained for title/abstract screening. Forty-two articles met the inclusion criteria and were accepted for full-text screening. Finally, 11 studies were included for quantitative analysis. The PRISMA flowchart summarizing the process of study screening in

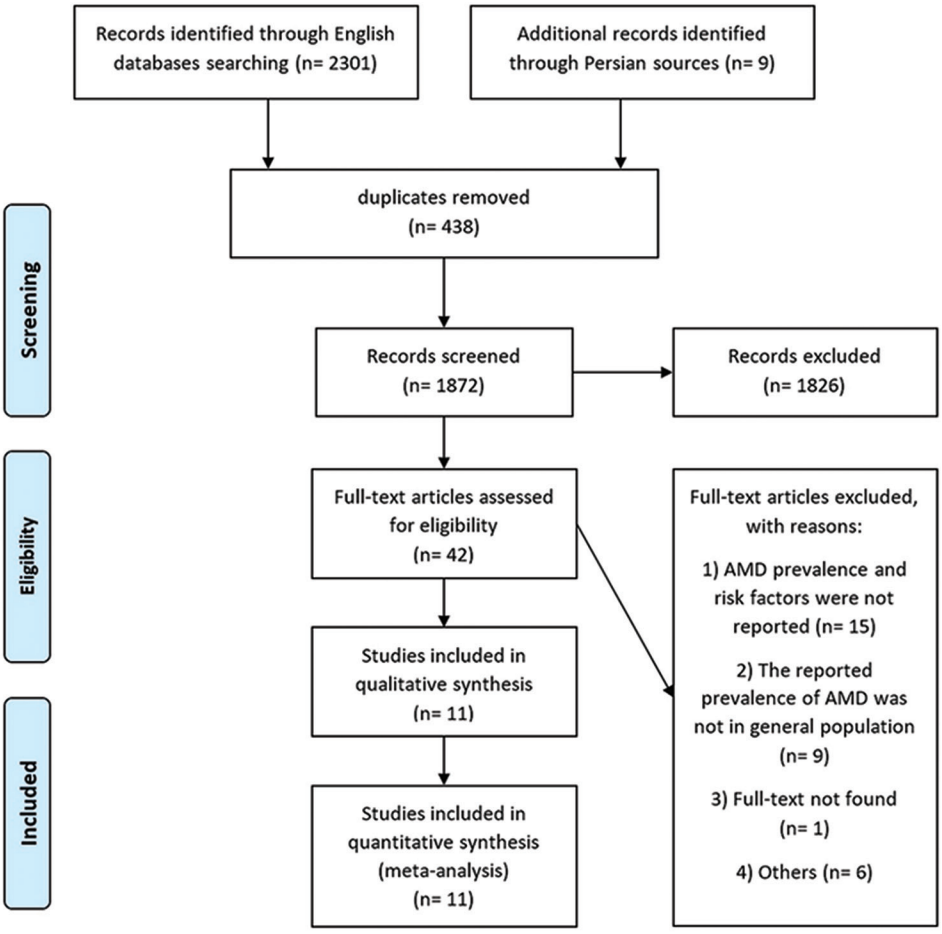

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses study selection flow diagram

this review is shown in Figure 1. All the included studies in meta-analysis were published between 2008 and 2021. Nine studies had a cross-sectional design, while two studies were case–control studies.[17-27] Four studies were conducted in Tehran and the others were conducted in Guilan, Shahroud, Sari, Yazd, Amirkola, Arak, and Shiraz. Table 1 summarizes the characteristics of the included studies.

Risk of bias and applicability

Table 2 indicates the results of NOS risk of bias assessment for the cross-sectional studies. Out of the nine selected studies with a cross-sectional design, two studies had acceptable quality.[19,25] Three studies had good quality and the rest had very good quality. In the course of patient selection, most of the studies did not report the characteristics of nonresponders, which is identified as a source of bias in NOS tool. Besides, the participants in the two studies with acceptable quality were not representative of the general population which is created another source of bias in the field of patient selection. In addition to these errors, failure to control confounding factors in the comparison between study groups was one of the major sources of bias in the studies with good and acceptable qualities. Unlike most of the cross-sectional studies, the two case–control studies included in the present meta-analysis had acceptable quality and received a score of only 5 from NOS tool. The main sources of bias in these studies were the noncommunity-based control groups, the mismatching for confounding variables between case and control groups, and the use of inappropriate methods to determine exposures [Table 3]. In conclusion, considering the sources of bias in the included studies, it can be noted that although the risk of bias for the pooled estimate of AMD prevalence was acceptable, the risk of bias in determining AMD risk factors was high.

Prevalence of age-related macular degeneration

Six studies that reported the prevalence of AMD in Iran were included in the meta-analysis to estimate pooled prevalence of the disease. The total sample size for the six studies was 9930. All participants were over 40 years old. The reported prevalence of AMD in these studies ranged from 4.7% to 17.6%. The pooled prevalence of AMD in Iran was estimated to be 9.9% (95% CI: 6.3%–13.5%). The heterogeneity between studies was meaningful (Q [df = 5] = 188.4, $P < 0.001$; $I^2 = 97.34\%$, $P < 0.001$). Figure 2 indicates the forest plot for the overall AMD prevalence estimate. Additional analyzes showed a significant publication bias (Egger's test, $P = 0.084$); therefore, the trim-and-fill method were implemented and the corrected pooled prevalence of AMD was estimated to be

Table 1: Summary of studies' characteristics included in the meta-analysis

Study*	Design	City	*n*†	Study population	Mean age	Sex (%)		AMD prevalence (%)	Included risk factors‡
						Male	Female		
Behboudi *et al*., 2020[20]	Cross-sectional	Guilan	2275	Residents >50 years old in rural and urban areas of Guilan	62.8	42	58	13.9	Male sex
Hashemi *et al*., 2015[21]	Cross-sectional	Shahroud	4387	Residents between 40 and 64 years of age in the urban areas of Shahrood	50.3	41.6	58.4	4.7	Smoking, male sex
Hashemi *et al*., 2017[22]	Cross-sectional	Sari	937	Residents >54 years old of Sari	64.7	46.3	53.7	5.8	-
Hatef *et al*., 2008[23§]	Cross-sectional	Tehran	1434	Residents >40 years old of Tehran	-	-	-	7.11	-
Katibeh *et al*., 2015[24]	Cross-sectional	Yazd	108	Residents between 40 and 84 years of age in the urban and rural areas of Yazd	-	32.4	67.6	-	Male sex
Nodehi-Moghadam *et al*., 2015[25]	Cross-sectional	Tehran	392	Residents >60 years old of Tehran	-	51.3	48.7	11.5	Male sex
Rajavi *et al*., 2011[26]	Cross-sectional	Tehran	275	Residents in southeastern of Tehran province	-	39.6	60.4	-	Male sex
Rasoulinejad *et al*., 2015[27]	Cross-sectional	Amirkola	505	Residents >60 years of Amirkola	71.55	57.4	42.6	17.6	Male sex, hyperlipidemia, smoking, DM, HTN
Akhgary *et al*., 2013[19]	Cross-sectional	Tehran	204	Patients who visited at low vision clinic	68	66.6	33.4	-	Male sex
Rezaei *et al*., 2012[17]	Case–control	Arak	300	Residents >50 years old of Arak	-	45	55	-	Male sex, hyperlipidemia, smoking, DM, HTN
Farvardin *et al*., 2021[18]	Case–control	Shiraz	180	Patients who visited at ophthalmology clinic	-	48.9	51.1	-	Hyperlipidemia, HTN, smoking

*First author and year of publication are mentioned in the table, †The number of subjects from each study included in the meta-analysis is reported, ‡Only risk factors from each study enrolled in the meta-analysis are reported in the table, §Only the data of patients over 40 years old in this study are reported in the table. DM: Diabetes mellitus, HTN: Hypertension, AMD: Age-related macular degeneration

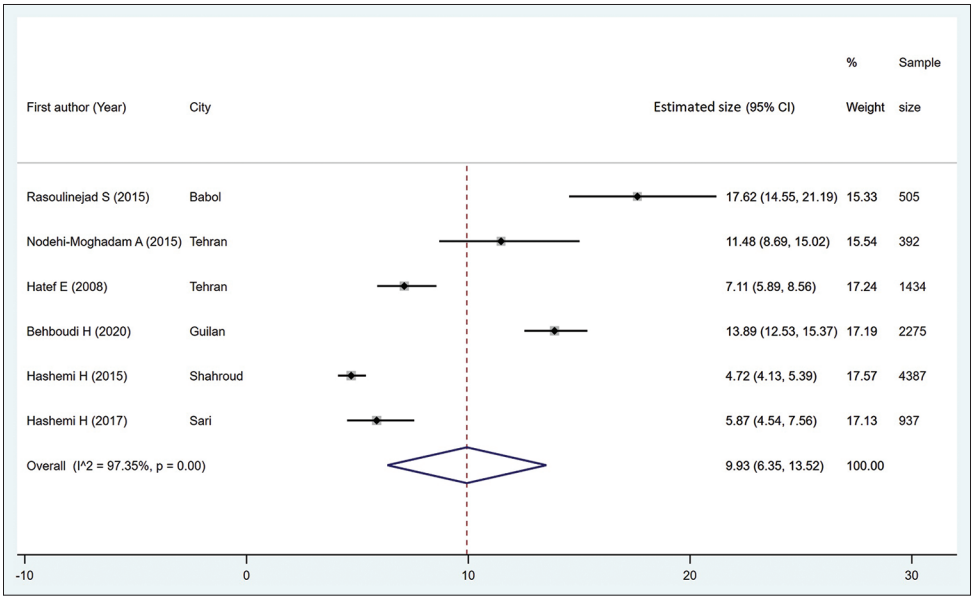

Figure 2: Forest plot for overall prevalence of age-related macular degeneration (percent) in Iran

Table 2: Risk of bias and applicability concerns summery for cross-sectional studies

Study	Selection				Comparability	Outcome		Total score	Role of the study in meta-analysis (prevalence or RF analysis)
	Representativeness	Sample size	Nonresponders	Ascertainment of exposure	Different outcome groups comparable	Assessment of outcome	Statistical test		
Behboudi *et al.*[20]	*	*	*	**	**	**	*	10	Prevalence and RF
Hashemi *et al.*[21]	*	*		**	**	**	*	9	Prevalence and RF
Hashemi *et al.*[22]	*	*		**	**	**	*	9	Prevalence
Hatef *et al.*[23]	*	*		**	**	**	*	9	Prevalence
Katibeh *et al.*[24]	*	*	*	**		**	*	8	RF
Nodehi-Moghadam *et al.*[25]				**		**	*	5	Prevalence and RF
Rajavi *et al.*[26]	*	*		**		**	*	7	RF
Rasoulinejad *et al.*[27]	*	*	*	**		**	*	8	Prevalence and RF
Akhgary *et al.*[19]		*		*		**	*	5	RF

RF: Risk factor

Table 3: Risk of bias and applicability concerns summery for case–control studies

Study	Selection				Comparability	Exposure			Total score	Role of the study in meta-analysis (prevalence RF analysis)
	Cases definition	Representativeness	Controls selection	Controls definition	Comparability of cases and controls	Ascertainment of exposures	Same method of ascertainment	Nonresponse rate		
Rezaei *et al.*[17]	*	*		*			*	*	5	RF
Farvardin *et al.*[18]	*	*		*			*	*	5	RF

RF: Risk factor

6.4% (95% CI: 4%–10.2%). Furthermore, meta-regression analysis demonstrated that independent variables including the mean age of the studies' samples ($P = 0.250$) and percentage of females ($P = 0.250$) did not have significant effects on the heterogeneity between studies. Finally, leave-one-out sensitivity analysis revealed that pooled prevalence of AMD was not meaningfully impacted by a single study.

Risk factors of age-related macular degeneration

Pooled effect of male sex, cigarette smoking, hypertension (HTN), diabetes mellitus (DM), and hyperlipidemia were estimated by *metan*. Table 4 summarizes the meta-analysis outcomes for these factors. Based on the results, smoking with OR: 1.781 (95% CI: 1.152–2.756), DM with OR: 1.545 (95% CI: 1.088–2.194), HTN with OR: 1.512 (95% CI: 1.119–2.044), and hyperlipidemia with OR: 1.512 (95% CI: 1.055–2.165) had significant effect on the incidence of AMD. While, male sex with OR: 0.977 (95% CI: 0.842–1.133) did not have significant effect on AMD occurrence [Supplementary Figures 1-5 indicate the forest plots for the pooled effect of the mentioned factors on AMD occurrence]. Additional analyzes indicated that there was no publication bias for all of the investigated factors, so there was no need to perform the trim-and-fill method. Furthermore, leave-one-out sensitivity analysis revealed no deviation from 95% CI for none of the risk factors. It should be noted that meta-regression analysis was not applicable due to the insufficient number of studies.

Discussion

According to the best of our knowledge, the present study is the first systematic review and meta-analysis on the prevalence and risk factors of AMD in Iran. A wide range (4.7%–17.6%) was reported for the prevalence of AMD in the included studies. This variation appears to be most likely due to differences in genetic and environmental factors in different geographic regions. The overall prevalence of AMD in patients over 40 years of age in Iran general population was estimated to be 9.9%, which decreased to 6.4% by considering the publication bias. Comparing the findings of this study with Wong *et al*.[7] meta-analysis, which reported an AMD global prevalence of 8.69%, reveals that the prevalence of this disease in Iran is slightly lower than the global average. In addition, this comparison demonstrates that AMD is less common in Iranian population than other races such as African (7.53%), Asian (7.38%), European (12.33%), and Hispanic (10.43%). It should be noted that although the AMD prevalence in Iran is estimated to be lower than the global prevalence, it is still necessary to pay special attention to this disease because it is one of the main causes of visual impairment in Iran, so that in the meta-analysis study conducted by Mohammadi *et al*.,[28] they introduced AMD as the fourth cause of visual impairment in Iran and estimated its prevalence 9.31% among people with visual impairment.

In addition to the prevalence of AMD, nongenetic risk factors of this disease in Iran were also investigated in the present study. The results of meta-analysis indicate that any history of smoking has the greatest effect on the AMD occurrence (OR = 1.781). This result is in agreement with previous studies that introduced smoking as the strongest modifiable risk factor for AMD.[1,29,30] In addition to smoking, HTN, DM, and hyperlipidemia were also identified as risk factors for AMD in Iran, according to the findings of this review. Although the results of previous studies confirm the role of dyslipidemia in AMD occurrence,[31-33] they have shown that DM and HTN do not have effect on the incidence of AMD, unlike the present study.[29,32,34,35] In explaining this disagreement, it should be noted that the results of the current meta-analysis about the effect of DM and HTN on AMD are not completely reliable because there were only a few number of studies with a moderate risk of bias (two studies for DM and three studies for HTN) to estimate the pooled effect of these factors on the AMD occurrence. Gender is the last factor that has been investigated in the present review. Similar to previous studies and meta-analyses,[5,29,32,35] the present results support the hypothesis that gender is not a risk factor for AMD. In addition to the mentioned factors, there are other risk factors that are not investigated in the current meta-analysis. One of these risk factors is age, which plays the most important role in developing AMD.[1,32] Although the effect of aging on the incidence of AMD was investigated in a number of studies conducted in Iran,[20-22,25] due to different age classification, it was not possible to combine the data of these studies to conduct a meta-analysis. Moreover, iris color,[17] history of cataract surgery,[17] Vitamin D deficiency,[36] high serum level of total cholesterol, triglyceride, and low-density lipoprotein[37] are the other factors that have been shown to be associated with AMD in previous Iranian studies, but they were not included in the meta-analysis due to limited data.

The primary strength of the current study lies in the inclusion of predominantly community-based studies (especially those reporting prevalence) with substantial sample sizes in the

Table 4: Results of meta-analysis for age-related macular degeneration risk factors

Investigated factor	Number of included studies	Pooled OR (95% CI)	I^2 (%), *P* of the heterogeneity test	*P* of the publication bias
Male sex	8	0.977 (0.842–1.133)	26.0, 0.221	0.759
Smoking	4	1.781 (1.152–2.756)	64.7, 0.037*	0.749
HTN	3	1.512 (1.119–2.044)	28.6, 0.246	0.573
DM	2	1.545 (1.088–2.194)	48.6, 0.163	N/A
Hyperlipidemia	3	1.512 (1.055–2.165)	37.1, 0.204	0.831

*Statistically significant. OR: Odds ratio, HTN: Hypertension, DM: Diabetes mellitus, N/A: Not applicable

meta-analysis. Nevertheless, the limited number of studies conducted in Iran concerning AMD impacts the precision of the present findings. To assess the overall prevalence of AMD, we aggregated data solely from four provinces, lacking information from the remaining 27 provinces. This omission could potentially lead to an inaccurate estimation of AMD's final prevalence in Iran. Furthermore, the diagnostic criteria for AMD were not consistently specified across the studies. Given the variation in diagnostic tools and methodologies employed in the included studies, the estimation of AMD prevalence within them may have been compromised, thus presenting another constraint within this study. An additional noteworthy limitation, as previously mentioned, is the absence of age classification for reported AMD cases in the studies. This absence has precluded the ability to report AMD prevalence within distinct age groups. It is worth noting that a comparable situation prevailed in determining the risk factors associated with AMD. Consequently, we combined data from a limited number of studies with varying degrees of bias to compute the pooled effect of these risk factors on AMD. As a result, there exists a need for more meticulously designed studies conducted across different provinces in Iran in the future. This is imperative to foster a more comprehensive understanding of the AMD landscape within Iran.

In conclusion, based on the results of this study, the prevalence of AMD in Iranian population is estimated to be 6.4%, which is slightly lower than the global prevalence. Furthermore, the results of meta-analysis indicated that having a history of smoking is the most important risk factor of AMD in Iran and HTN, DM, and hyperlipidemia should be considered the other risk factors of the disease. However, it is necessary to conduct more original studies in the future for obtaining more accurate and more definitive conclusions.

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Conflicts of interest
There are no conflicts of interest.

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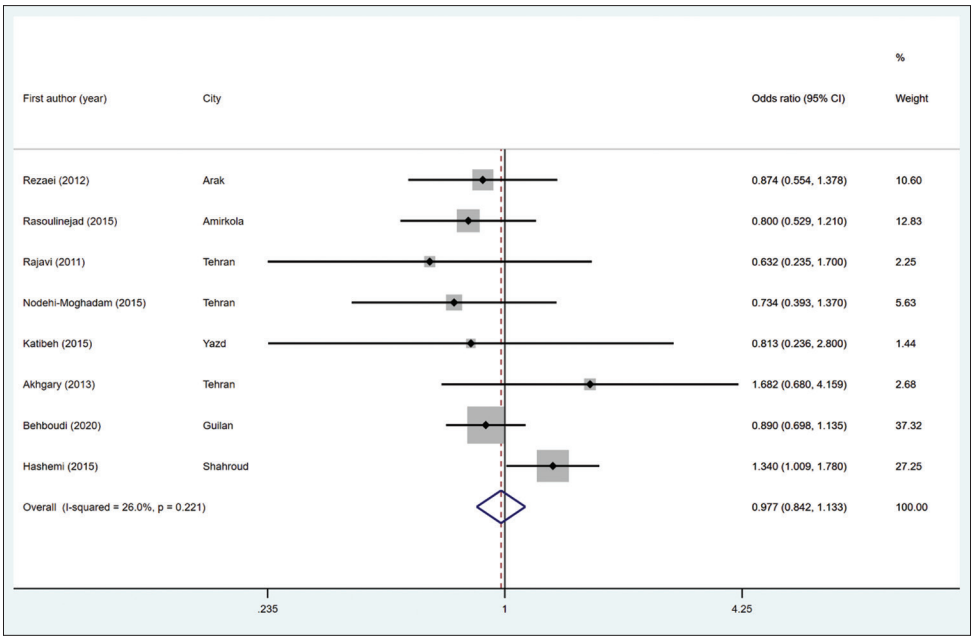
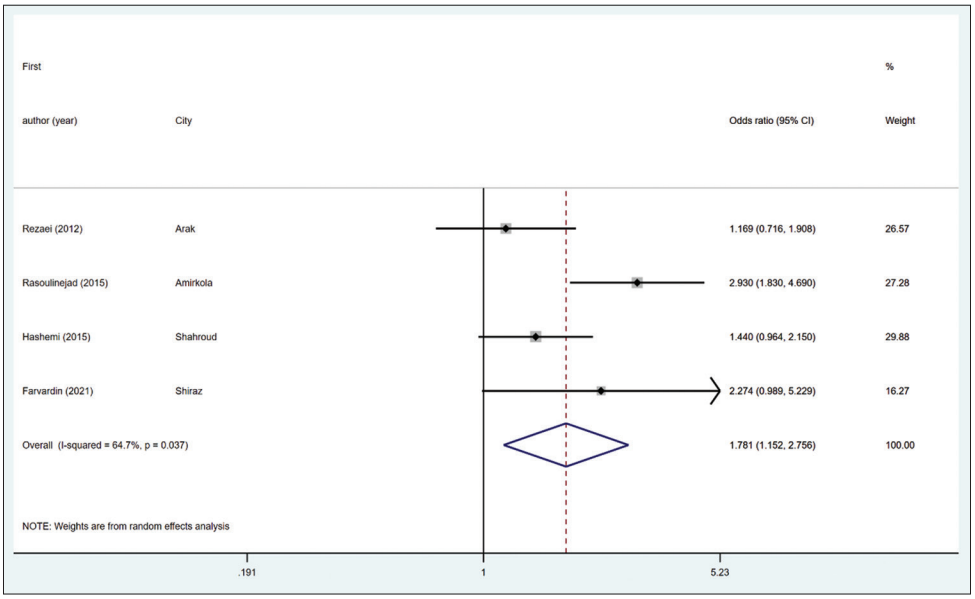
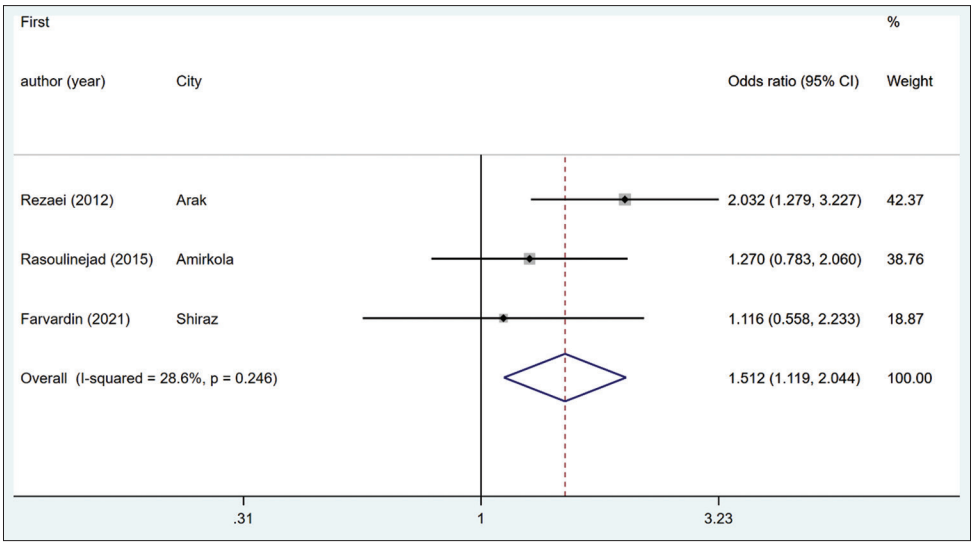


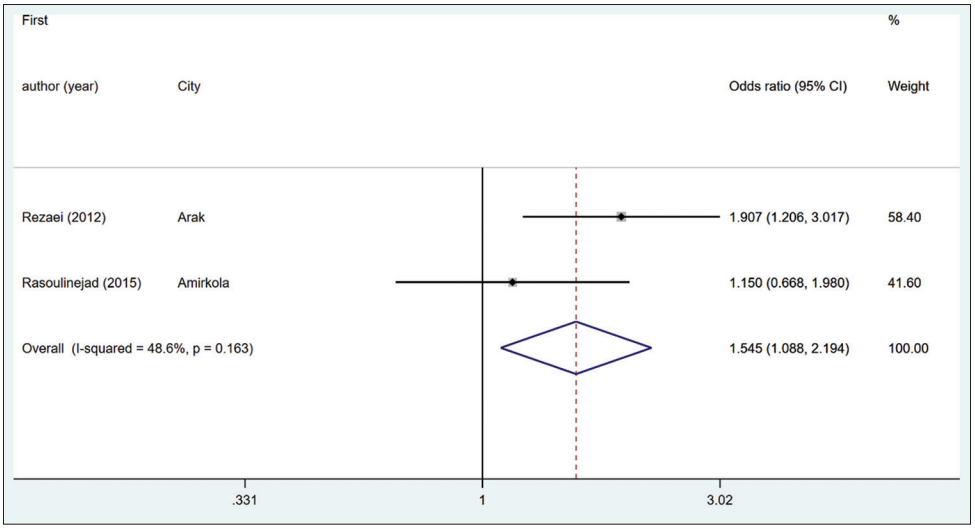
Supplementary Figure 1: Forest plot for pooled estimated effect of sex male on age-related macular degeneration occurrence



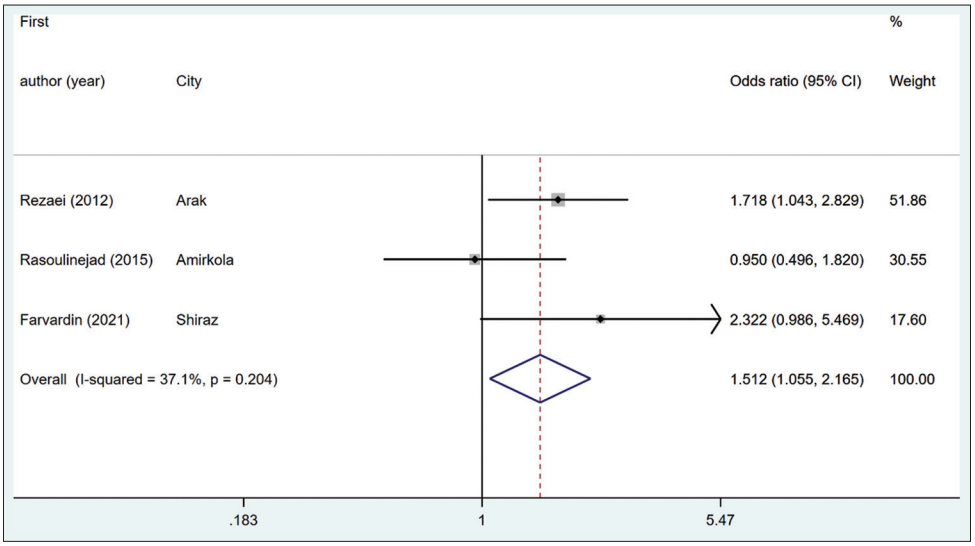
Supplementary Figure 2: Forest plot for pooled estimated effect of smoking on age-related macular degeneration occurrence



Supplementary Figure 3: Forest plot for pooled estimated effect of hypertension on age-related macular degeneration occurrence



Supplementary Figure 4: Forest plot for pooled estimated effect of diabetes mellitus on age-related macular degeneration occurrence



Supplementary Figure 5: Forest plot for pooled estimated effect of hyperlipidemia on age-related macular degeneration occurrence

Supplementary Table 1: Full search strategy for PubMed

Database	Search strategy
PubMed	(“Macular Degeneration”[Mesh] OR “Geographic Atrophy”[Mesh] OR “Wet Macular Degeneration”[Mesh] OR “Degeneration, Macular” OR “Macular Degenerations” OR “Maculopathy” OR “Maculopathies” OR “Age-Related Macular Degeneration” OR “Age Related Macular Degeneration” OR “Age-Related Macular Degenerations” OR “Macular Degeneration, Age-Related” OR “Macular Degeneration, Age Related” OR “Maculopathies, Age-Related” OR “Maculopathy, Age-Related” OR “Maculopathy, Age Related” OR “Age-Related Maculopathies” OR “Age Related Maculopathies” OR “Age-Related Maculopathy” OR “Age Related Maculopathy” OR “Atrophies, Geographic” OR “Atrophy, Geographic” OR “Geographic Atrophies” OR “Dry Macular Degeneration” OR “Degeneration, Dry Macular” OR “Degenerations, Dry Macular” OR “Dry Macular Degenerations” OR “Macular Degeneration, Dry” OR “Macular Degenerations, Dry” OR “Degeneration, Wet Macular” OR “Degenerations, Wet Macular” OR “Macular Degeneration, Wet” OR “Macular Degenerations, Wet” OR “Wet Macular Degenerations” OR “Neovascular Age-Related Macular Degeneration” OR “Neovascular Age Related Macular Degeneration” OR “Neovascular Age-Related Macular Degenerations” OR “Non-neovascular Age-Related Macular Degeneration” OR “Non-neovascular Age Related Macular Degeneration” OR “Non-neovascular Age-Related Macular Degenerations” OR “Atrophic Age-Related Macular Degeneration” OR “Atrophic Age Related Macular Degeneration” OR “Atrophic Age-Related Macular Degenerations” OR “Atrophic Macular Degeneration” OR “Non-neovascular Macular Degenerations” OR “Neovascular Macular Degeneration”) AND (“Prevalence”[Mesh] OR “Epidemiology”[Mesh] OR “Incidence”[Mesh] OR “Health Care Survey”[Mesh] OR “Health Survey”[Mesh] OR “Demography”[Mesh] OR “Surveys and Questionnaires”[Mesh] OR “Cross-Sectional Studies”[Mesh] OR “Cohort Studies”[Mesh] OR “Case-Control Studies”[Mesh] OR “Retrospective Studies”[Mesh] OR “Prospective Studies”[Mesh] OR “Risk Factors”[Mesh] OR “Myopia”[Mesh] OR “Myopia, Degenerative”[Mesh] OR “Hyperopia”[Mesh] OR “Diabetes Mellitus”[Mesh] OR “Diabetes Complications”[Mesh] OR “Diabetes Mellitus, Type 2”[Mesh] OR “Diabetes Mellitus, Type 1”[Mesh] OR “Hypertension”[Mesh] OR “Hyperlipidemias”[Mesh] OR “Smoking”[Mesh] OR “Cigarette Smoking”[Mesh] OR “Cigar Smoking”[Mesh] OR “Diet”[Mesh] OR “Alcohol Drinking”[Mesh] OR “Sex”[Mesh] OR “Male”[Mesh] OR “Female”[Mesh] OR “Age Groups”[Mesh] OR “Prevalences” OR “Period Prevalence” OR “Period Prevalences” OR “Prevalence, Period” OR “Point Prevalence” OR “Point Prevalences” OR “Prevalence, Point” OR “Social Epidemiology” OR “Epidemiologies, Social” OR “Epidemiology, Social” OR “Social Epidemiologies” OR “Incidences” OR “Secondary Attack Rate” OR “Attack Rate, Secondary” OR “Rate, Secondary Attack” OR “Secondary Attack Rates” OR “Incidence Proportion” OR “Incidence Proportions” OR “Proportion, Incidence” OR “Attack Rate” OR “Attack Rates” OR “Rate, Attack” OR “Cumulative Incidence” OR “Cumulative Incidences” OR “Incidence, Cumulative” OR “Incidence Rate” OR “Incidence Rates” OR “Rate, Incidence” OR “Person-time Rate” OR “Person time Rate” OR “Person-time Rates” OR “Rate, Person-time” OR “Factor, Risk” OR “Risk Factor” OR “Social Risk Factors” OR “Factor, Social Risk” OR “Factors, Social Risk” OR “Risk Factor, Social” OR “Risk Factors, Social” OR “Social Risk Factor” OR “Health Correlates” OR “Correlates, Health” OR “Population at Risk” OR “Populations at Risk” OR “Risk Scores” OR “Risk Score” OR “Score, Risk” OR “Risk Factor Scores” OR “Risk Factor Score” OR “Score, Risk Factor” OR “None-genetic Risk Factors”) AND (“Iran”[Mesh] OR “Iran”[AD] OR “Iran”)

Supplementary Table 2: Full search strategy for Scopus

Database	Search strategy
Scopus	(ALL (“Macular Degeneration”) OR ALL (“Geographic Atrophy”) OR ALL (“Wet Macular Degeneration”) OR ALL (“Degeneration, Macular”) OR ALL (“Macular Degenerations”) OR ALL (“Maculopathy”) OR ALL (“Maculopathies”) OR ALL (“Age-Related Macular Degeneration”) OR ALL (“Age Related Macular Degeneration”) OR ALL (“Age-Related Macular Degenerations”) OR ALL (“Macular Degeneration, Age-Related”) OR ALL (“Macular Degeneration, Age Related”) OR ALL (“Maculopathies, Age-Related”) OR ALL (“Maculopathy, Age-Related”) OR ALL (“Maculopathy, Age Related”) OR ALL (“Age-Related Maculopathies”) OR ALL (“Age Related Maculopathies”) OR ALL (“Age-Related Maculopathy”) OR ALL (“Age Related Maculopathy”) OR ALL (“Atrophies, Geographic”) OR ALL (“Atrophy, Geographic”) OR ALL (“Geographic Atrophies”) OR ALL (“Dry Macular Degeneration”) OR ALL (“Degeneration, Dry Macular”) OR ALL (“Degenerations, Dry Macular”) OR ALL (“Dry Macular Degenerations”) OR ALL (“Macular Degeneration, Dry”) OR ALL (“Macular Degenerations, Dry”) OR ALL (“Degeneration, Wet Macular”) OR ALL (“Degenerations, Wet Macular”) OR ALL (“Macular Degeneration, Wet”) OR ALL (“Macular Degenerations, Wet”) OR ALL (“Wet Macular Degenerations”) OR ALL (“Neovascular Age-Related Macular Degeneration”) OR ALL (“Neovascular Age Related Macular Degeneration”) OR ALL (“Neovascular Age-Related Macular Degenerations”) OR ALL (“Non-neovascular Age-Related Macular Degeneration”) OR ALL (“Non-neovascular Age Related Macular Degeneration”) OR ALL (“Non-neovascular Age-Related Macular Degenerations”) OR ALL (“Atrophic Age-Related Macular Degeneration”) OR ALL (“Atrophic Age Related Macular Degeneration”) OR ALL (“Atrophic Age-Related Macular Degenerations”) OR ALL (“Atrophic Macular Degeneration”) OR ALL (“Non-neovascular Macular Degenerations”) OR ALL (“Neovascular Macular Degeneration”)) AND (ALL (“Prevalence”) OR ALL (“Epidemiology”) OR ALL (“Incidence”) OR ALL (“Health Care Survey”) OR ALL (“Health Survey”) OR ALL (“Demography”) OR ALL (“Surveys and Questionnaires”) OR ALL (“Cross-Sectional Studies”) OR ALL (“Cohort Studies”) OR ALL (“Case-Control Studies”) OR ALL (“Retrospective Studies”) OR ALL (“Prospective Studies”) OR ALL (“Risk Factors”) OR ALL (“Myopia”) OR ALL (“Myopia, Degenerative”) OR ALL (“Hyperopia”) OR ALL (“Diabetes Mellitus”) OR ALL (“Diabetes Complications”) OR ALL (“Diabetes Mellitus, Type 2”) OR ALL (“Diabetes Mellitus, Type 1”) OR ALL (“Hypertension”) OR ALL (“Hyperlipidemias”) OR ALL (“Smoking”) OR ALL (“Cigarette Smoking”) OR ALL (“Cigar Smoking”) OR ALL (“Diet”) OR ALL (“Alcohol Drinking”) OR ALL (“Sex”) OR ALL (“Male”) OR ALL (“Female”) OR ALL (“Age Groups”) OR ALL (“Prevalences”) OR ALL (“Period Prevalence”) OR ALL (“Period Prevalences”) OR ALL (“Point Prevalence”) OR ALL (“Point Prevalences”) OR ALL (“Prevalence, Point”) OR ALL (“Social Epidemiology”) OR ALL (“Epidemiologies, Social”) OR ALL (“Epidemiology, Social”) OR ALL (“Incidences”) OR ALL (“Secondary Attack Rate”) OR ALL (“Attack Rate, Secondary”) OR ALL (“Rate, Secondary Attack”) OR ALL (“Secondary Attack Rates”) OR ALL (“Incidence Proportion”) OR ALL (“Incidence Proportions”) OR ALL (“Proportion, Incidence”) OR ALL (“Attack Rate”) OR ALL (“Attack Rates”) OR ALL (“Rate, Attack”) OR ALL (“Cumulative Incidence”) OR ALL (“Cumulative Incidences”) OR ALL (“Incidence, Cumulative”) OR ALL (“Incidence Rate”) OR ALL (“Incidence Rates”) OR ALL (“Rate, Incidence”) OR ALL (“Person-time Rate”) OR ALL (“Person time Rate”) OR ALL (“Person-time Rates”) OR ALL (“Rate, Person-time”) OR ALL (“Factor, Risk”) OR ALL (“Risk Factor”) OR ALL (“Social Risk Factors”) OR ALL (“Factor, Social Risk”) OR ALL (“Factors, Social Risk”) OR ALL (“Risk Factor, Social”) OR ALL (“Risk Factors, Social”) OR ALL (“Social Risk Factor”) OR ALL (“Health Correlates”) OR ALL (“Correlates, Health”) OR ALL (“Population at Risk”) OR ALL (“Populations at Risk”) OR ALL (“Risk Scores”) OR ALL (“Risk Score”) OR ALL (“Score, Risk”) OR ALL (“Risk Factor Scores”) OR ALL (“Risk Factor Score”) OR ALL (“Score, Risk Factor”) OR ALL (“None-genetic Risk Factors”)) AND (ALL (“Iran”))

Supplementary Table 3: Full search strategy for Web of Science

Database	Search strategy
Web of Science	(“Macular Degeneration”[Mesh] OR “Geographic Atrophy”[Mesh] OR “Wet Macular Degeneration”[Mesh] OR “Degeneration, Macular” OR “Macular Degenerations” OR “Maculopathy” OR “Maculopathies” OR “Age-Related Macular Degeneration” OR “Age Related Macular Degeneration” OR “Age-Related Macular Degenerations” OR “Macular Degeneration, Age-Related” OR “Macular Degeneration, Age Related” OR “Maculopathies, Age-Related” OR “Maculopathy, Age-Related” OR “Maculopathy, Age Related” OR “Age-Related Maculopathies” OR “Age Related Maculopathies” OR “Age-Related Maculopathy” OR “Age Related Maculopathy” OR “Atrophies, Geographic” OR “Atrophy, Geographic” OR “Geographic Atrophies” OR “Dry Macular Degeneration” OR “Degeneration, Dry Macular” OR “Degenerations, Dry Macular” OR “Dry Macular Degenerations” OR “Macular Degeneration, Dry” OR “Macular Degenerations, Dry” OR “Degeneration, Wet Macular” OR “Degenerations, Wet Macular” OR “Macular Degeneration, Wet” OR “Macular Degenerations, Wet” OR “Wet Macular Degenerations” OR “Neovascular Age-Related Macular Degeneration” OR “Neovascular Age Related Macular Degeneration” OR “Neovascular Age-Related Macular Degenerations” OR “Non-neovascular Age-Related Macular Degeneration” OR “Non-neovascular Age Related Macular Degeneration” OR “Non-neovascular Age-Related Macular Degenerations” OR “Atrophic Age-Related Macular Degeneration” OR “Atrophic Age Related Macular Degeneration” OR “Atrophic Age-Related Macular Degenerations” OR “Atrophic Macular Degeneration” OR “Non-neovascular Macular Degenerations” OR “Neovascular Macular Degeneration”) AND (“Prevalence”[Mesh] OR “Epidemiology”[Mesh] OR “Incidence”[Mesh] OR “Health Care Survey”[Mesh] OR “Health Survey”[Mesh] OR “Demography”[Mesh] OR “Surveys and Questionnaires”[Mesh] OR “Cross-Sectional Studies”[Mesh] OR “Cohort Studies”[Mesh] OR “Case-Control Studies”[Mesh] OR “Retrospective Studies”[Mesh] OR “Prospective Studies”[Mesh] OR “Risk Factors”[Mesh] OR “Myopia”[Mesh] OR “Myopia, Degenerative”[Mesh] OR “Hyperopia”[Mesh] OR “Diabetes Mellitus”[Mesh] OR “Diabetes Complications”[Mesh] OR “Diabetes Mellitus, Type 2”[Mesh] OR “Diabetes Mellitus, Type 1”[Mesh] OR “Hypertension”[Mesh] OR “Hyperlipidemias”[Mesh] OR “Smoking”[Mesh] OR “Cigarette Smoking”[Mesh] OR “Cigar Smoking”[Mesh] OR “Diet”[Mesh] OR “Alcohol Drinking”[Mesh] OR “Sex”[Mesh] OR “Male”[Mesh] OR “Female”[Mesh] OR “Age Groups”[Mesh] OR “Prevalences” OR “Period Prevalence” OR “Period Prevalences” OR “Prevalence, Period” OR “Point Prevalence” OR “Point Prevalences” OR “Prevalence, Point” OR “Social Epidemiology” OR “Epidemiologies, Social” OR “Epidemiology, Social” OR “Social Epidemiologies” OR “Incidences” OR “Secondary Attack Rate” OR “Attack Rate, Secondary” OR “Rate, Secondary Attack” OR “Secondary Attack Rates” OR “Incidence Proportion” OR “Incidence Proportions” OR “Proportion, Incidence” OR “Attack Rate” OR “Attack Rates” OR “Rate, Attack” OR “Cumulative Incidence” OR “Cumulative Incidences” OR “Incidence, Cumulative” OR “Incidence Rate” OR “Incidence Rates” OR “Rate, Incidence” OR “Person-time Rate” OR “Person time Rate” OR “Person-time Rates” OR “Rate, Person-time” OR “Factor, Risk” OR “Risk Factor” OR “Social Risk Factors” OR “Factor, Social Risk” OR “Factors, Social Risk” OR “Risk Factor, Social” OR “Risk Factors, Social” OR “Social Risk Factor” OR “Health Correlates” OR “Correlates, Health” OR “Population at Risk” OR “Populations at Risk” OR “Risk Scores” OR “Risk Score” OR “Score, Risk” OR “Risk Factor Scores” OR “Risk Factor Score” OR “Score, Risk Factor” OR “None-genetic Risk Factors”) AND (“Iran”[Mesh] OR “Iran”[AD] OR “Iran”)

Supplementary Table 4: Full search strategy for Google Scholar

Database	Search strategy
Google Scholar	(“Macular Degeneration” OR “Wet Macular Degeneration” OR “Age-Related Macular Degeneration” OR “Dry Macular Degeneration”) AND (“Prevalence” OR “Epidemiology” OR “Incidence” OR “Health Care Survey” OR “Demography” OR “Risk Factors”) AND (“Iran”)