



Prevalence of Glaucoma in Iran: a systematic review and meta-analysis

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Background: Glaucoma is a late-onset incurable disease and the major cause of incurable blindness in the world. Since Iran is in Asia, and has the highest number of glaucoma patients in the world, the disease should be followed in a particular manner. **Purpose:** The present systematic review and meta-analysis was conducted with the aim of evaluating the prevalence of glaucoma in Iran. **Methods:** The prevalence of glaucoma is defined using international criteria and measured as the main outcome. Study selection, data extraction, and quality assessment were performed by two independent reviewers. PubMed, EMBASE, ISI Web of science, Scopus and national databases (SID, MAGIRAN) were searched for observational studies which evaluated the prevalence of glaucoma in the Iranian population from 1995 to July 2017. The meta-analysis method was used to estimate the overall prevalence. Hoi j tools were used for the quality assessment of studies. **Results:** Of the 199 studies evaluated, 24 studies included meta-analysis. In 2017, the pooled overall prevalence of glaucoma in 35596 people was 3.75% (95% CI: 3.12, 4.37, I²=96.16%). Based on the sub-group analysis in the random effect method, the prevalence of glaucoma in males and females were 3.57% (95% CI: 2.83, 4.32), and 2.52% (95% CI: 2.39, 3.27). **Conclusion:** Considering the high prevalence of glaucoma in Iran relative to regional and global standards, these findings can be used by health policymakers as the basis for planning decisions for the prevention, treatment, and examination of glaucoma patients in Iran.

INTRODUCTION

Glaucoma is a late-onset incurable disease and the major cause of incurable blindness in the world (1). Based on the American Academy of Ophthalmology standards (Table 1), there are several types of glaucoma (2). The most common forms are Primary Open-Angle Glaucoma (POAG) and Primary Angle-Closure Glaucoma (PACG). POAG is the most common type of glaucoma in the world, as it accounts for 3% of the global prevalence of glaucoma (3.54%). Today, there are more than 64.3 million people with glaucoma in the world. With a projected increase of 18.3% in 2020 and 74% in 2040 as compared with 2013, it is estimated that the number of people with glaucoma would respectively reach more than 76 million people and 111.8 million people. Although the global prevalence of glaucoma is 3.54%, its prevalence in Asia exceeds 6.5%. More than 51 million (60%) glaucoma patients live in Asia (3), where more than 33.45 million people have been diagnosed with POAG (4). The most remarkable

points about glaucoma include: the possibility of disease development in everyone, lack of symptoms at the early stages which are highly important in timely diagnosis of the disease, and low awareness of people about the disease (5-7). The major causes and sub-factors responsible for glaucoma include old age, a family history of glaucoma, elevated intraocular pressure, and low systolic pressure (8). Since Iran is in Asia, and has the highest number of glaucoma patients in the world, the disease should be followed in a particular manner. With respect to limited funds and human resources of the health system, determination of the precise prevalence of major diseases may considerably help policy-makers to perform appropriate planning and futuristic policy-making. Based on the most recent knowledge of the researcher, no systematic review has ever been conducted in this field. This study was designed to assess the prevalence of glaucoma in Iran.

METHODS

Registration and Eligibility criteria

The methods adopted for this systematic review were developed in accordance with the guidelines detailed on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (9). The protocol of this systematic review has been registered in PROSPERO 2017 (Registration Number: [CRD42017076643](https://www.crd42017076643)), (10). It included observational studies, including Cross-sectional (Descriptive, Analytical), Case-control (retrospective, prospective, case-cohort, nested) and Cohort (retrospective, prospective and historical). This study

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Table 1 Types of glaucoma based on the American Academy of Ophthalmology standards

Overall Classification	Type of glaucoma	Definition
OPEN-ANGLE GLAUCOMA	1. Primary open-angle glaucoma (POAG)	• not associated with known ocular or systemic disorders that cause increased resistance to aqueous outflow or damage to optic nerve • usually associated with elevated IOP
	2. Normal-tension glaucoma	• considered in continuum of POAG; often used when IOP is not elevated
	3. Juvenile open-angle glaucoma	• used when open-angle glaucoma diagnosed at young age (typically 10-30 years of age)
	4. Glaucoma suspect	• normal optic disc and visual field associated with elevated IOP • suspicious optic disc and/or visual field with normal IOP
	5. Secondary open-angle glaucoma	• increased resistance to trabecular meshwork outflow associated with other conditions (e.g. pigmentary-, phacolytic-, steroid-induced-) • increased posttrabecular resistance to outflow secondary to elevated episcleral venous pressure (e.g. carotid cavernous sinus fistula)
B. Angle-Closure Glaucoma	1. Primary ACG with relative pupillary block	• movement of aqueous humor from posterior chamber to anterior chamber restricted • peripheral iris in contact with trabecular meshwork
	2. Acute angle closure	• occurs when IOP rises rapidly as a result of relatively sudden blockage of the trabecular meshwork
	3. Subacute angle closure (intermittent angle closure)	• repeated, brief episodes of angle closure with mild symptoms and elevated IOP, often a prelude to acute angle closure
	4. Chronic angle closure	• IOP elevation caused by variable portions of anterior chamber angle being permanently closed by PAS
	5. Secondary ACG with pupillary block	• e.g. swollen lens, secluded pupil
	6. Secondary ACG without pupillary block	• posterior pushing mechanism: lens-iris diaphragm pushed forward (e.g. posterior segment tumor, scleral buckling procedure, uveal effusion) • anterior pulling mechanism: anterior segment process pulling iris forward to form PAS (e.g. iridocorneal endothelial syndrome, neovascular glaucoma, inflammation)
	7. Plateau iris syndrome	• primary angle closure with or without component of pupillary block, but pupillary block is not predominant mechanism of angle closure
C. Childhood Glaucoma	1. Primary congenital/infantile glaucoma	• primary glaucoma present from birth to first few years of life
	2. Glaucoma associated with congenital anomalies	• associated with ocular disorders (e.g. anterior segment dysgenesis, aniridia) • associated with systemic disorders (e.g. rubella, Lowe syndrome)
	3. Secondary glaucoma in infants and children	• e.g. glaucoma secondary to retinoblastoma or trauma

excluded case series, case reports, clinical trials, and reviews (systematic review, narrative reviews). Participants: The researchers included all studies which were conducted on the general population and patients with vision problems and are at least in one group-sex included. Outcome: The prevalence of glaucoma was measured in this study. Glaucoma was defined as the presence of at least two of the following three criteria: (1) glaucomatous changes in the optic nerve head including cup-to-disc ratio (C/D) of 0.6 or more, C/D asymmetry of more than 0.2, rim notching or splinter hemorrhages on or adjacent to the optic nerve head; (2) IOP higher than 22 mmHg; and (3) the presence of at least two of the following in the visual field tests (11, 12). The minimum required sample size was ≥ 25 patients. The setting of the studies included a hospital and a community.

Sources of information and search strategy

Literature search strategies were developed using medical subject headings (MeSH) and text words related to glaucoma prevalence in Iran. Electronic databases were searched including international databases (PubMed, EMBASE, Web of science, Scopus), national databases (scientific information database (SID) and Magiran), Key Journal (Journal of Current Ophthalmology) and other sources. To ensure

literature saturation, the reference lists of included studies or relevant reviews identified through the search were scanned. No setting and language limits were imposed on the search. The specific search strategies were created by a Health Sciences Librarian with expertise in systematic review searching. The MEDLINE strategy was developed with input from the project team, then peer reviewed by a second librarian, not otherwise associated with the project, using the Peer Review of Electronic Search Strategies (PRESS) standard (13). After finalizing the MEDLINE strategy, it was adapted to the syntax and subject headings of the other databases. Also, PROSPERO was used to search for ongoing or recently completed systematic reviews. The key words were Glaucoma, Prevalence, Population and Iran that combine with Boolean operators including (AND .OR).

Data management and study selection

The results of literature search were uploaded to Endnote Software. Based on the inclusion and exclusion criteria, the team developed and tests screening questions and forms for level 1 and 2 assessments. Citation abstracts and full text articles were uploaded with screening questions to Endnote. Prior to the formal screening process, a calibration exercise was undertaken to pilot and refine the screening questions. A

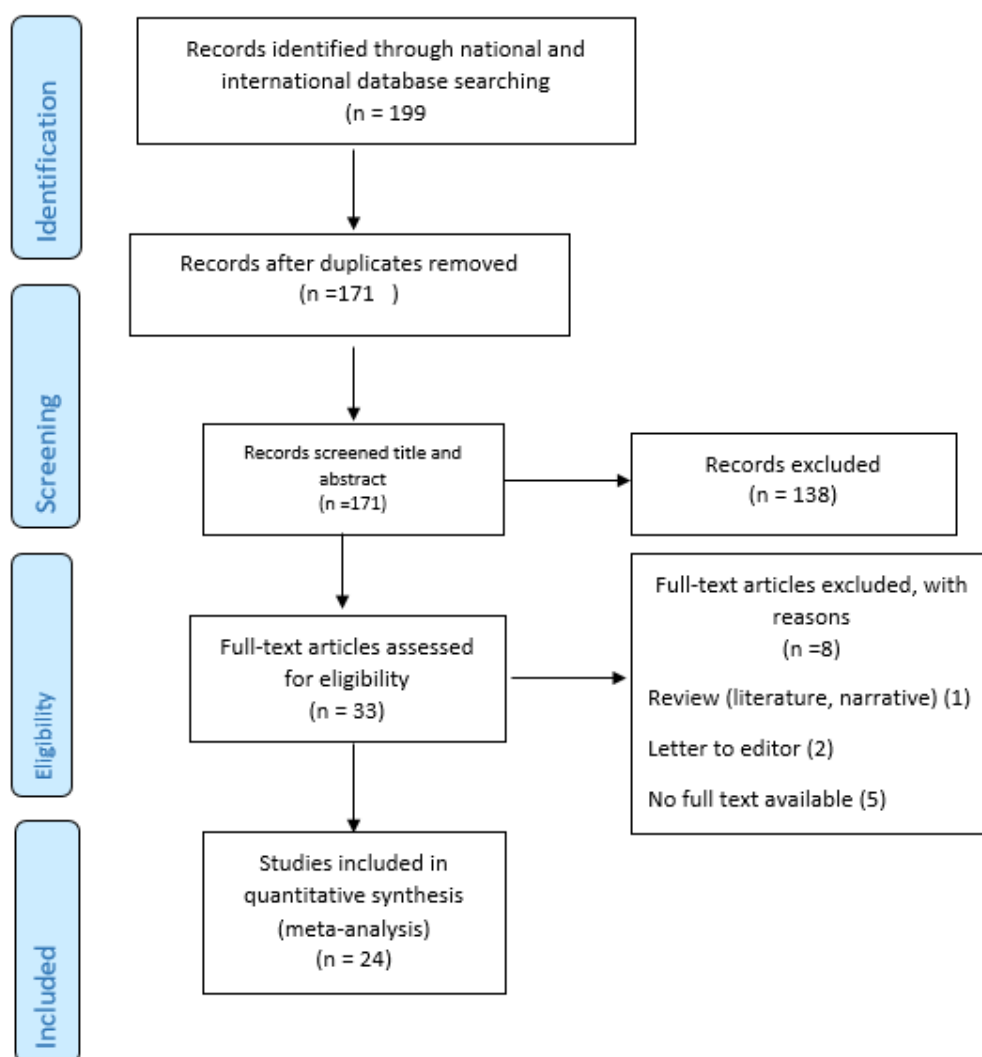


Figure 1 Flow diagram of article selection process

formal screening process was conducted by two researchers and the consensus method was used to solve controversies among two researchers. The two reviewers independently screened the titles and abstracts and relied on the eligibility criteria. Full reports were obtained for all titles that seemed to meet the inclusion criteria. To resolve questions about eligibility, additional information was sought from the authors of the study. The reasons for excluding studies were recorded. Neither of the review authors was blinded to the journal titles or to the study authors or institutions.

Data Extraction and Quality assessment

A data extraction form was developed and study data assessed and extracted independently by two reviewers. To ensure consistency across reviewers, calibration exercises were conducted prior to the commencement of the review. A consensus method was used to solve controversies among the two researchers. The extracted data items were general information (authors, title, source and year of publication), Study characteristics (Study design, Participant characteristics (demographics, sample size) and Outcome measures (Prevalence of glaucoma). To assess the quality of studies, Hoy et al.'s tools were utilized (14). These judgments were made independently by two review

authors based on the criteria for judging the risk of bias, where there is disagreement; the consensus method should be used to solve controversies.

Data synthesis

All the eligible studies were included in synthesis after systematic review. Forest plot was used for combination of data. The overall prevalence of glaucoma was estimated by the random-effects model. The heterogeneity of preliminary studies was determined by I² Test. Sub-group analysis was conducted for diagnosis of heterogeneity based on the kind of study participants and sex. Meta-analysis was performed using STAT 12 Statistics software.

RESULTS

Study selection

A total of 24 articles, conducted on 35,596 people, were entered into the final stage of the study. The list of studies is available at [http://uploadboy.me/j2ux8dmu3i6b/List of papers.docx.html](http://uploadboy.me/j2ux8dmu3i6b/List%20of%20papers.docx.html). The search identified 171 non-duplicated potentially eligible studies in 22 years from 1995 to July 2017. After a detailed review of titles and abstracts, a total of 33 full text articles were reviewed. The eligibility criteria were

Table 2 Summary of included studies

ID	Author (year)	Province	Sampling Method	Design	Setting	Sample size	Age	Study Duration	Risk of bias
1	Akhgari, M(2014)(1)	Tehran	Simple Random Sampling (SRS)	Cross-Sectional	Hospital	204	45.2	1(y)	Moderate
2	Amini, H.(2007)(23)	Tehran	Stratified Sampling	Cross-Sectional	Health Center	2184	55.1	1(y)	low
3	Behrouzi, Z(2007)(24)	Tehran	Convenience Sampling	Cross-Sectional	Private Eye Clinic	237	39.1	4(m)	low
4	Besharati, M(2006)(25)	Yazd	Census	Cross-Sectional	Welfare Centre	109	24.6	9(m)	low
5	Faeze, K(2016)(26)	Gilan	Purposive Sampling	Retrospective Descriptive	Hospital	100	67.7	1(y)	low
6	Feghhi, M(2009)(27)	Khuzestan	Multistage Sampling	Cross-Sectional	Health Center	6960	24.7	1(y)	low
7	Hashemi, H(2017)(28)	Mazandaran	Cluster Sampling	Cross-Sectional	Health center	937	64.7	1(y)	low
8	Khalaj, M(2013)(29)	Qazvin	Simple Random Sampling (SRS)	Cross-Sectional	Hospital	446	62.9	1(y)	low
9	Khataminia, G(2010)(30)	Khuzestan	Census	Retrospective Descriptive	Hospital	283	44	6(y)	Moderate
10	Maeiat, M(2013)(31)	Ardabil	Convenience Sampling	Cross-Sectional	Welfare Centre	403	33.2	7(m)	low
11	Masumi, R(2012)(32)	Ardabil	convenience sampling	Cross-Sectional	Hospital	300	66.7	1(y)	low
12	Medghalchi, A(2002)(33)	Fars	Purposive Sampling	Cross-Sectional	Hospital	42	34.4	3(y)	Moderate
13	Mirdehghan, S. A.(2005)(34)	Tehran	Convenience Sampling	Cross-Sectional	Hospital	362	13.5	1(y)	low
14	NodehiMoghadam, A(2015)(35)	Tehran	Purposive Sampling	Cross-Sectional	Private Eye Clinic	392	71.6	2(y)	low
15	Ostadi-Moghaddam, H(2007)(36)	Khorasan Razavi	Purposive Sampling	Cross-Sectional	School	286	14.2	4(m)	Moderate
16	Pakravan, M(2013)(37)	Yazd	Cluster Sampling	Cross-Sectional	Private Eye Clinic	2098	54.1	2(y)	low
17	Rajavi, J(2003)(38)	Tehran	Convenience Sampling	Cross-Sectional	Hospital	92	11.4	10(y)	Moderate
18	Reaei, A(2003)(39)	Tehran	Cluster Sampling	Cross-Sectional	Private Eye Clinic	2160	55.1	2(y)	High Risk
19	Sadaghipour, M(2002)(40)	Azerbaijan Gharbi	Census	Cross-Sectional	Hospital	310	18.2	1(y)	Moderate
20	Shahriari, H. A(2007)(41)	Sistan v Balouchistan	Cluster Sampling	Cross-Sectional	Hospital	5446	31.1	1.5(y)	low
21	Sharifi, N(2009)(42)	Azerbaijan Sharghi	Simple Random Sampling (SRS)	Cross-Sectional	Private Eye Clinic	500	40.5	6(m)	low
22	Soori, H(2011)(43)	Tehran	Cluster Sampling	Cross-Sectional	Hospital	10702	27.7	1(y)	low
23	Tavalloli, A(2006)(44)	Azerbaijan Gharbi	Cluster Sampling	Cross-Sectional	Hospital	440	55.1	1(y)	Moderate
24	Yaqubi, G(2004)(45)	Khorasan Jonobi	Census	Cross-Sectional	Hospital	523	67.2	7(y)	low

applied and 9 articles were excluded (reasons summarized in Figure 1) with a total of 24 articles meeting the inclusion criteria. Of the 24 included studies, 22 studies provided only cross-sectional data, 2 studies provided only retrospective descriptive data (Figure 1).

Study and participants' characteristics

Studies were conducted by 31 professors in 13 provinces. Most studies were carried out in Tehran province (n=8) and the least number in Ardebil, Khuzestan and Yazd provinces (1 study). (With a population of 80 million, Iran is located in the eastern Mediterranean region in west Asia and consists of 32 provinces.) Most studies were descriptive-cross-sectional (n=22), utilized a cluster sampling method (n=6), and were performed in hospitals (n=13). The mean duration of studies was 1.8 years. The mean age of participants was 44 years and most of them were female (n=20405; 57.4%). Table 2 presents most of the studies.

Meta-analysis prevalence of glaucoma

Based on the results of the random effect method, the overall prevalence of glaucoma in 35596 people was 3.75% (95% CI: 3.12, 4.37, $I^2=96.16\%$), (Figure 2). Sub-group analysis was done for diagnosis of heterogeneity based on the kind of study participants and sex. The prevalence of glaucoma was four times more in people with vision problems than the general population. Therefore, the pool estimated (in

random model) prevalence of glaucoma in the general population and in people with vision problems were 2.23% (95% CI: 1.62, 2.84, $I^2=95.40\%$) and 9.0% (95% CI: 6.32, 11.67, $I^2=95.43\%$), respectively (Figure 2). Based on sub-group analysis in the random effect method, the prevalence of glaucoma in males and females were 3.57% (95% CI: 2.83, 4.32, $I^2=92.54\%$) and 2.52% (95% CI: 2.39, 3.27, $I^2=92.29\%$), respectively. This difference was also found in the sub-group of study participants (Table 3). Further, a sensitivity test found that age group restricted participants estimated pooled prevalence for glaucoma; So, prevalence of general population were 1.81% (95% CI: 1.21, 2.42%) and 3.95% (95% CI: 0.0, 8.40%) in under and over 60 years old, respectively; and in at-risk population (people with vision problems) were 7.73% (95% CI: 4.89, 10.56%) and 13.21% (95% CI: 2.31, 24.11%), respectively (Figure 3).

Meta-regression finding

The proportion of glaucoma was estimated at 3.75% (95% CI: 3.12, 4.37, $I^2=96.16\%$) (Table2). In meta-regression, the study participants variable significantly contributed to heterogeneity with Coef.=6.64 (95% CI: 2.33, 10.95), $\tau^2=25.9$ Adj R-squared=28.59. Although, there was a non-statistically significant linear trend in univariate meta-regression to explain effect size variation by age in terms of the mean age of study (P -Value=0.588). Also, meta-regression in sub-group of participants not

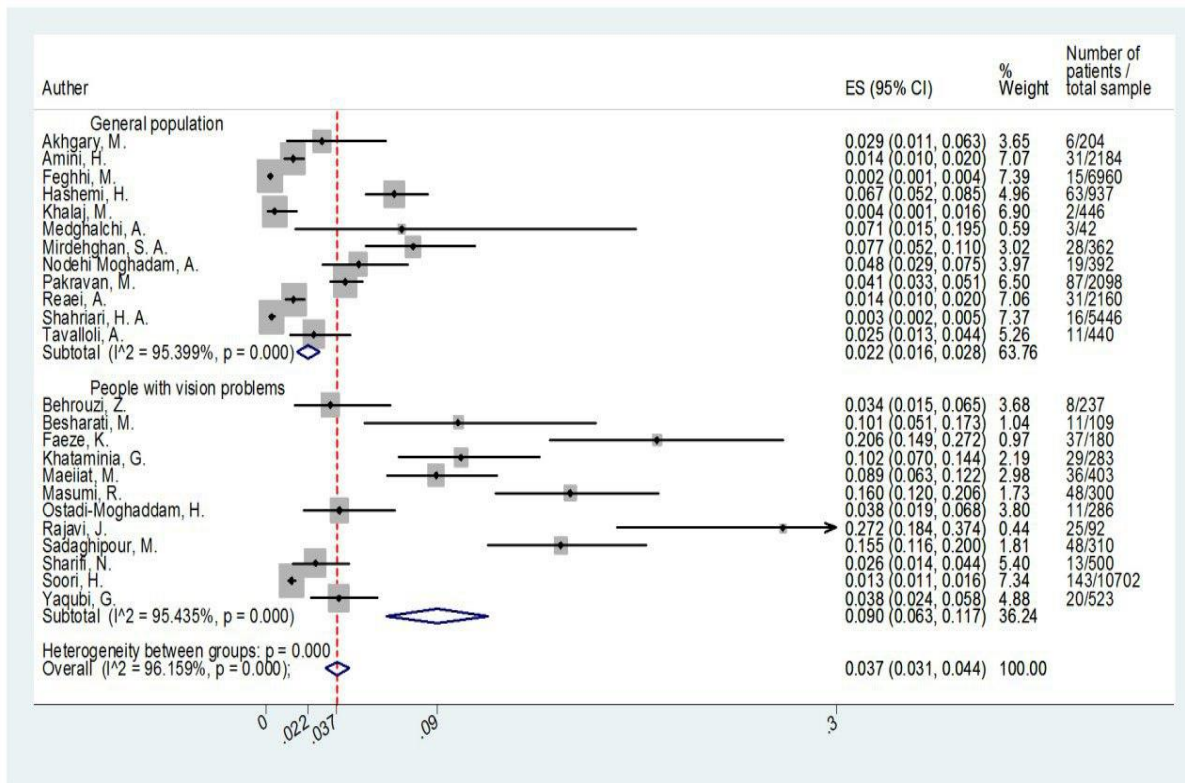


Figure 2 Pooled analyses and subgroup analyses by study population for estimation the overall prevalence of glaucoma

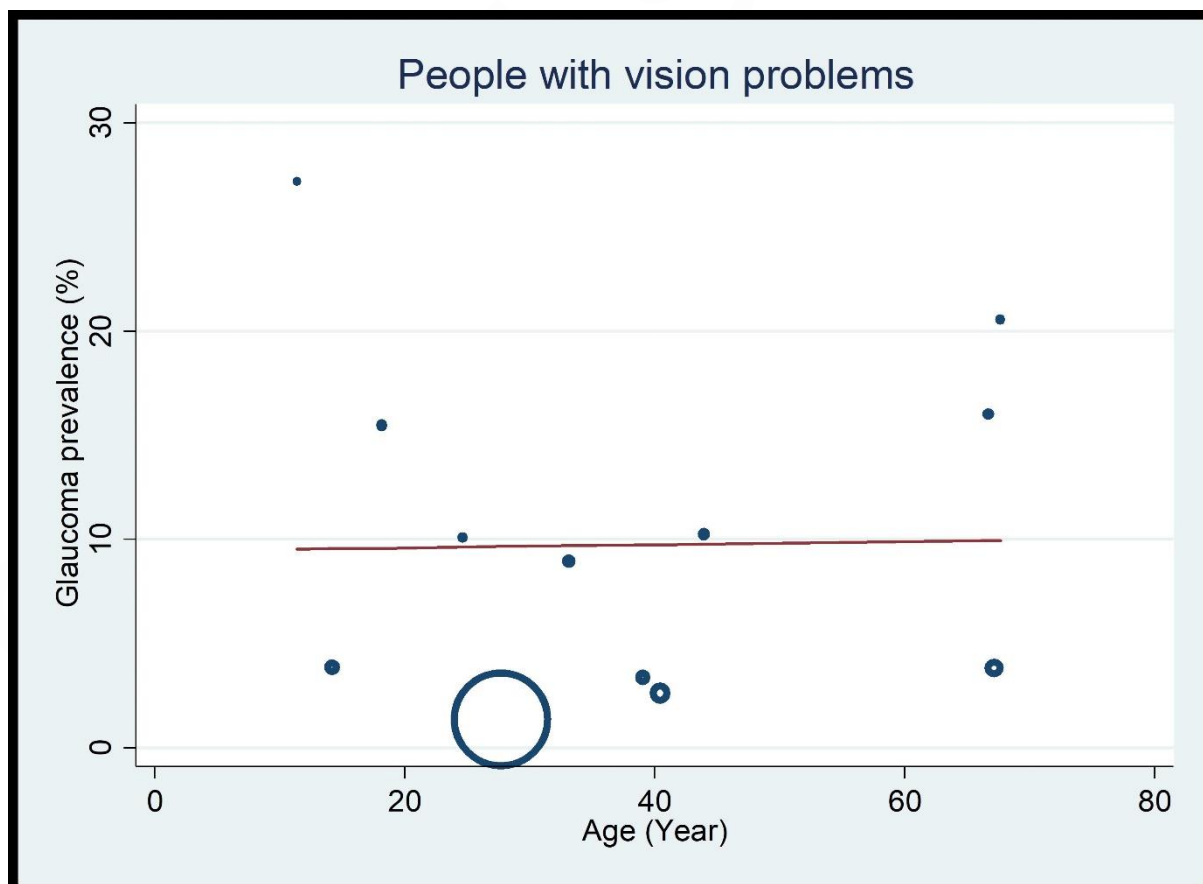


Figure 3 Meta-regression between age (year) and the prevalence of glaucoma in people with vision problems in Iran

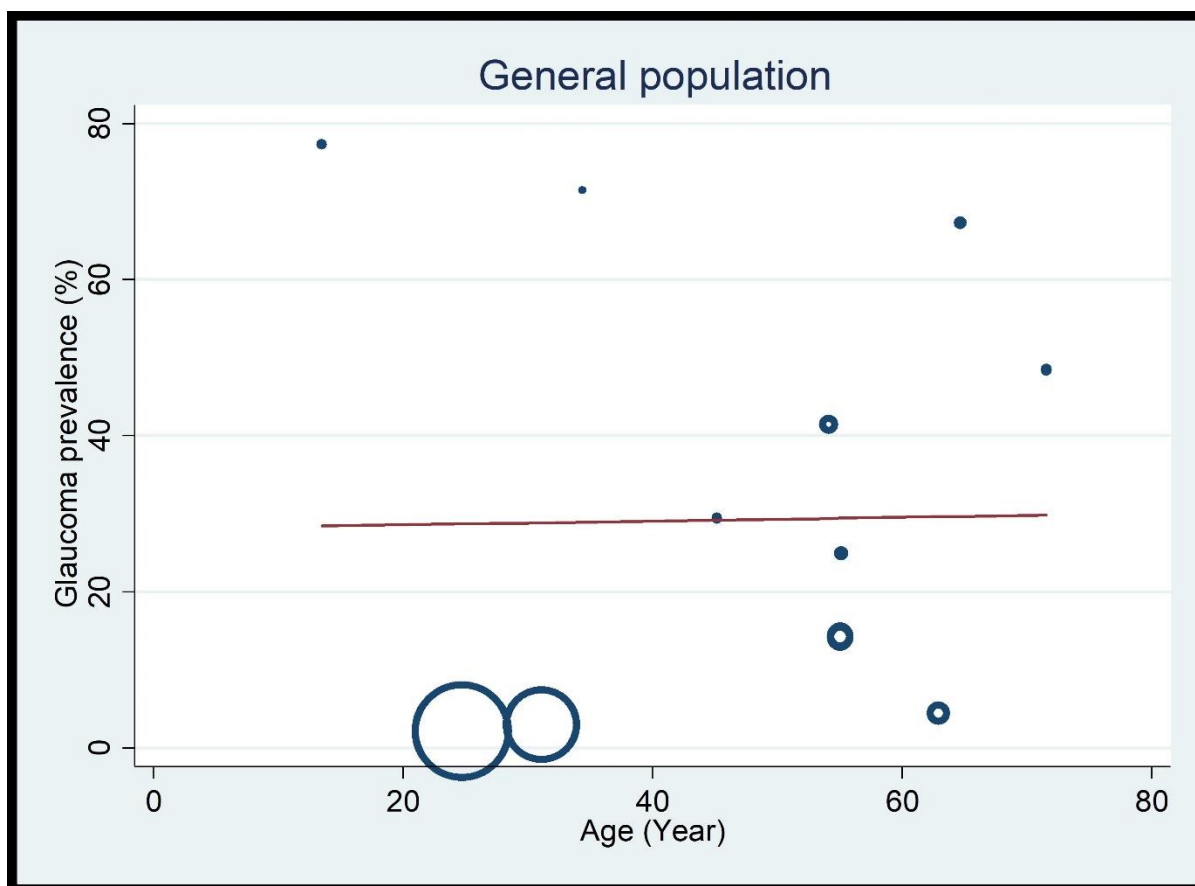


Figure 4 Meta-regression between age (year) and the prevalence of glaucoma in general population in Iran

Table 3 Sub-group analysis based on type of study participants and sex

		Male			Female		
ID	First author	ES	95% CI for ES	% Wight	ES	95% CI for ES	% Wight
General population							
1	Akhgary, M. (1)	5.71	1.58 to 13.99	1.53	1.49	0.18 to 5.29	4.58
2	Amini, H. (23)	2.21	1.32 to 3.47	7.3	0.97	0.52 to 1.65	8.87
6	Feghhi, M. (27)	0.28	0.12 to 0.56	8.38	0.17	0.07 to 0.35	9.44
7	Hashemi, H. (28)	6.9	4.7 to 9.7	4.53	6.57	4.57 to 9.11	4.32
8	Khalaj, M. (29)	0.41	0.01 to 2.26	7.68	0.5	0.01 to 2.73	7.66
12	Medghalchi, A. (33)	6.25	0.77 to 20.81	0.72	10	0.25 to 44.5	0.11
13	Mirdehghan, S. A. (34)	4.76	2.31 to 8.58	3.73	11.84	7.17 to 18.07	1.23
14	NodehiMoghadam, A.(35)	5.47	2.76 to 9.58	3.37	4.19	1.83 to 8.09	3.11
16	Pakravan, M. (37)	4.01	2.84 to 5.49	6.78	4.68	3.49 to 6.13	6.73
18	Reaei, A. (39)	2.21	1.32 to 3.47	7.3	0.97	0.52 to 1.65	8.87
20	Shahriari, H. A. (41)	0.26	0.09 to 0.56	8.38	0.32	0.15 to 0.59	9.39
23	Tavalloli, A. (44)	2.02	0.55 to 5.09	5.32	2.89	1.17 to 5.87	4.44
Sub-total Random pooled ES		2.14	1.43 to 2.85	65.03	1.71	1.11 to 2.32	68.73
People with vision problems							
3	Behrouzi, Z. (24)	5.08	1.06 to 14.15	1.46	3.14	1.03 to 7.19	3.30
4	Besharati, M. (25)	9.59	3.94 to 18.76	1.06	11.11	3.11 to 26.06	0.34
5	Faeze, K. (26)	27.16	17.87 to 38.19	0.55	15.15	8.74 to 23.76	0.69
9	Khataminia, G. (30)	7.41	3.89 to 12.58	2.43	14.05	8.4 to 21.54	0.88
10	Maeiiat, M. (31)	7.79	4.75 to 11.89	3.1	8.81	4.9 to 14.33	1.60
11	Masumi, R. (32)	16.37	11.16 to 22.79	1.48	15.5	9.73 to 22.92	0.87
15	Ostadi-Moghaddam, H. (36)	1.91	0.4 to 5.48	4.97	6.2	2.72 to 11.85	1.75
17	Rajavi, J. (38)	23.26	11.76 to 38.63	0.33	30.61	18.25 to 45.42	0.22
19	Sadaghipour, M. (40)	15.56	11.36 to 20.59	2.11	15.09	6.75 to 27.59	0.38
21	Sharifi, N. (42)	4.26	2.22 to 7.32	4.57	0.46	0.01 to 2.53	7.87
22	Soori, H. (43)	1.28	0.96 to 1.67	8.29	1.37	1.1 to 1.68	9.29
24	Yaqubi, G. (45)	4.21	2.19 to 7.24	4.62	3.36	1.46 to 6.52	4.06
Sub-total Random pooled ES		8.51	5.57 to 11.45	34.97	6.78	4.69 to 3.13	31.27
Overall Random pooled ES		3.57	2.83 to 4.32	100	2.52	1.91 to 3.13	100

showed significant heterogeneity effect (P -Value>0.05) (Figure 2, 3). In multivariate meta-regression, still participants variable was significant (P -Value=0.018) but age was not significant (P -Value=0.924) (Figure 4).

DISCUSSION

Glaucoma is a major cause of blindness in the world and there has been an increase in its occurrence in the last decade. Over 60% of this growth has been particularly pronounced in developing Asian countries (3). The present systematic review study includes cross-sectional and retrospective descriptive studies on the prevalence of glaucoma over the past 21 years which were performed on 35,596 people. (Iran is one of the countries located in west Asia). According to the main results of this study, the prevalence of glaucoma in Iran is 3.75%. The results of a study by Chan showed that the prevalence of glaucoma is 3.40% in west Asia and 3.54% in Asia, indicating the higher prevalence of glaucoma in Iran than Asia (4). According to population-based studies in different countries, the prevalence of glaucoma is 1.73% in Qatar (15), 0.94% in Nepal (16), 3.40% in Singapore (17), and 1.62% in India (18), all lower than Iran. However, the prevalence of glaucoma in Oman (4.75), (19) and Thailand (3.80%), (20) are higher when compared to Iran. These differences can be attributed to the sample size in various studies, mostly performed with a sample size of between 1000 and 3000, and to sampling accuracy and error possibility in population studies. Other reasons include access to ophthalmic examinations and knowledge on ocular diseases (21). The results of this study showed that the prevalence of glaucoma in people with visual problems is four times that of healthy people, highlighting the role of ocular diseases history, especially glaucoma (22). In this study, the prevalence of glaucoma was 1.41 times higher in men (3.57%) as compared to women (2.52%), which is similar to the overall prevalence ratio of glaucoma in Asia (1.47), (4). Based on the knowledge of the researchers, this is the first systematic review study on this topic in Iran. In addition, a meta-analysis approach was used in order to summarize the results of the studies. Moreover, most of the studies used had a good methodology and patients were selected based on proper inclusion criteria. Most studies lacked demographic information, necessitating communication with the article's author and requesting information that slowed down the work. The most important limitation of studies was their geographic location, most of which were carried out in Tehran province. All studies were conducted in 13 provinces, and there was no information on the prevalence of glaucoma in other provinces.

CONCLUSION

Considering the increasing trend of glaucoma in the world, especially in Asia, and the obtained results, which indicate the high prevalence of glaucoma in Iran relative to regional and global standards, these findings can be used by health policymakers as the basis for planning decisions for the prevention, treatment, and examination of glaucoma patients in Iran. Finally, national studies are recommended to consider all areas of the country in order to provide more accurate information for policymakers.

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