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REVIEW

Impact of Environmental Factors on Glaucoma Progression: A Systematic Review

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Background: Glaucoma, a leading cause of irreversible vision loss, is characterized by progressive degeneration of retinal ganglion cells. Intraocular pressure (IOP) remains a well-established risk factor, but recent research suggests environmental and lifestyle factors may also play a role.

Objective: This review aimed to evaluate the current evidence on the impact of environmental factors on glaucoma progression.

Methods: We conducted a systematic review following PRISMA guidelines, searching various databases for studies on environmental factors and glaucoma progression.

Results: Our review identified several key findings. IOP remains the most crucial modifiable risk factor. Aerobic exercise and mindfulness practices may lower IOP and provide neuroprotection. Lifestyle modifications like smoking cessation and balanced diets were also emphasized. Studies suggest air pollution exposure, particularly PM2.5, may be associated with an increased risk of glaucoma. However, the studies were primarily observational, and more research is needed to establish causality and elucidate underlying mechanisms.

Conclusion: This review highlights the multifaceted nature of glaucoma, emphasizing the interplay between established risk factors (IOP) and emerging environmental influences (air pollution). Environmental factors hold promise as potential targets for glaucoma prevention and management strategies. Future research should focus on well-designed studies to investigate causal relationships and biological mechanisms.

Keywords: glaucoma, intraocular pressure, IOP, environmental factors, air pollution, lifestyle modifications, aerobic exercise, diet, public health

Introduction

Glaucoma is a leading cause of irreversible blindness globally.[1] It is characterized by damage to the optic nerve and loss of visual field and is often associated with elevated intraocular pressure (IOP). Despite advancements in diagnostic and therapeutic approaches, understanding the multifactorial pathogenesis of glaucoma, involving genetic predisposition, ocular factors, and environmental influences, remains crucial.[2,3] Increasingly, research has emphasized the impact of environmental factors on glaucoma progression, alongside genetic susceptibility and ocular parameters.

Environmental factors such as lifestyle choices, occupational exposures, geographical variations, socioeconomic disparities, and climatic conditions are pivotal in influencing the risk of developing glaucoma and its severity and progression.[4–6] Factors, including smoking, alcohol consumption, diet, physical activity levels, and exposure to air pollution, have been associated with the onset and progression of glaucoma through mechanisms such as oxidative stress, inflammation, and neurodegeneration.

The significance of environmental factors as modifiable risk factors highlights the importance of preventive interventions and personalized treatment strategies. Performing a systematic literature review on the impact of environmental factors on glaucoma progression is essential for synthesizing current evidence, identifying research gaps, and elucidating underlying mechanisms. By comprehensively analysing available data, this study aims to provide insights into the complex interplay between environmental exposures and glaucoma pathogenesis, thereby enhancing clinical management and patient outcomes.

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In summary, investigating the influence of environmental factors on glaucoma progression is crucial for advancing our understanding of the disease and optimizing therapeutic approaches. Integrating genetic, ocular, and environmental factors in a comprehensive framework can improve risk assessment, facilitate early detection, and enable targeted interventions for individuals at risk of glaucoma-related vision loss. This systematic review provides valuable insights to advance glaucoma research and guide future investigations into the environmental determinants of disease progression.

Aims & Objectives

To conduct a systematic review of published studies investigating the association between environmental factors and glaucoma progression, focusing on both epidemiological and mechanistic research by evaluating the methodological quality of the included studies, including study design, sample size, data collection methods, and statistical analyses, to ensure the validity and reliability of the findings.

Methodology

Search Strategy

Figure 1 depicts the PRISMA flowchart, a standardized reporting guideline to improve the transparency and reproducibility of systematic reviews and meta-analyses.[7] This flowchart outlines the study selection process, from the initial search to the final

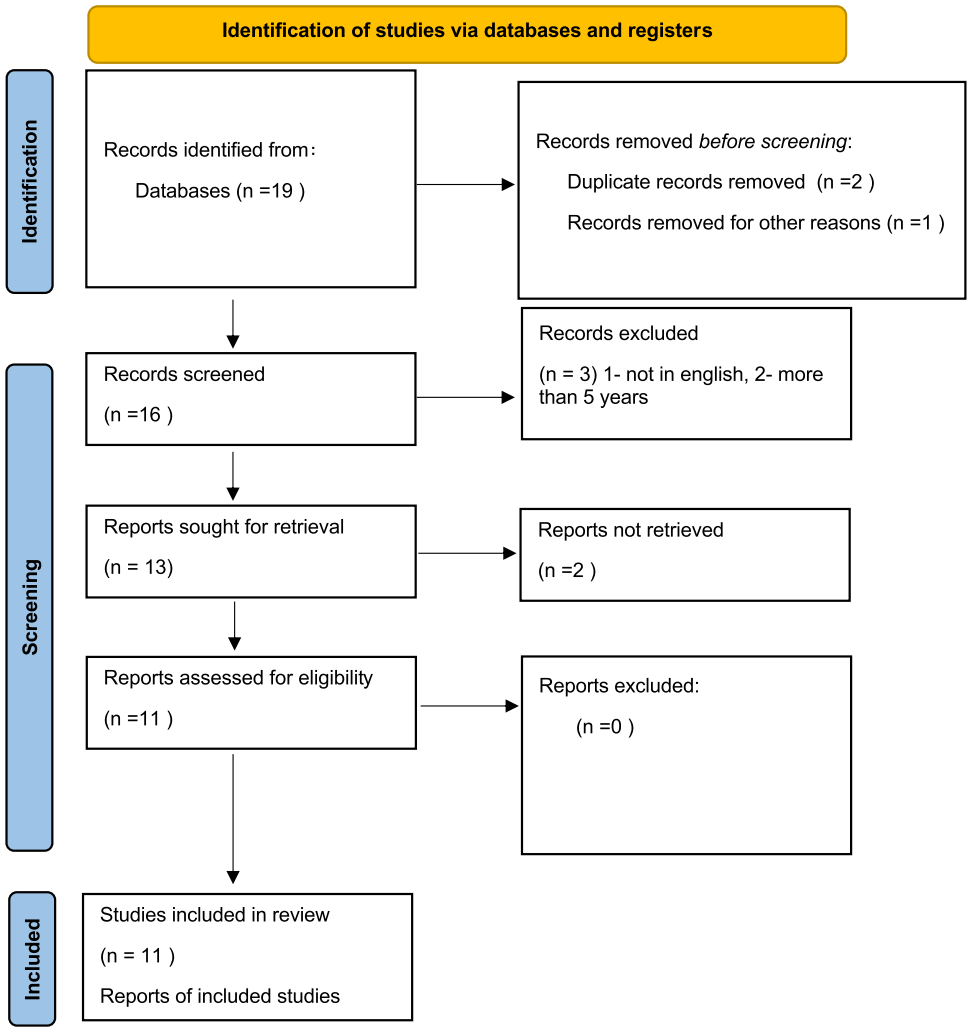

Figure 1 The PRISMA flowchart.
Notes: Adapted from Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: n71[7].

included studies. A comprehensive and systematic search was conducted to identify studies evaluating the impact of environmental factors on glaucoma progression. The following databases were searched: PubMed, MEDLINE, Embase, Cochrane Library, CINAHL, and relevant grey literature sources. The search was limited to articles published in English from January 2000 to May 2024. Keywords and Medical Subject Headings (MeSH) terms included "glaucoma", "environmental factors", "progression", "air pollution", "temperature", "humidity", "light exposure", and "socioeconomic factors".

Inclusion and Exclusion Criteria

Inclusion Criteria

Studies that investigated the relationship between environmental factors and glaucoma progression,

Peer-reviewed articles, including observational studies (cohort, case-control, and cross-sectional) and clinical trials,

Studies with clearly defined diagnostic criteria for glaucoma, and studies that provided quantitative measures of glaucoma progression (eg, changes in intraocular pressure, visual field loss, or optic nerve damage).

Exclusion Criteria

Articles that did not focus on environmental factors,

Studies without clear definitions of glaucoma progression,

Editorials, and case reports, and all non-English publications.

Data Extraction

Data were extracted independently by two reviewers using a standardized data extraction form. The following information was collected:

Study characteristics: author, year of publication, country, study design.

Participant characteristics: sample size, age, gender, glaucoma type.

Environmental factors: type of exposure (eg, air pollution, temperature), duration and intensity of exposure.

Outcomes: measures of glaucoma progression (eg, intraocular pressure, visual field analysis, optic nerve assessment).

Results: main findings related to the impact of environmental factors on glaucoma progression.

Discrepancies between reviewers were resolved through discussion, and if necessary, a third reviewer was consulted.

Quality Assessment

The assessment focused on:

Selection bias: representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure, and demonstration that outcome of interest was not present at the start of the study.

Comparability: control for confounding factors.

Outcome assessment: method of outcome assessment, follow-up duration, and adequacy of follow-up.

Ethical Considerations

As this study involved a review of published data, no ethical approval was required. However, the review adhered to ethical standards for systematic reviews, including transparency, rigor, and reproducibility.

Results

Table 1 presents eleven studies on glaucoma management and risk factors. Rivera et al[8] highlight risk factors for primary open-angle glaucoma progression and call for further research. Kumar et al.[9] In their study focused on intraocular pressure reduction through pharmacological and surgical therapies and lifestyle factors like aerobic exercise, mindfulness, caffeine, and nicotinamide supplementation. Leske et al[10] emphasize treatment and IOP reduction in mitigating glaucoma progression. Perez et al[11] emphasize the importance of lifestyle, exercise, and nutrition in preventing or slowing glaucoma progression. Hecht et al[12] discussed the benefits of moderate aerobic exercise and a high-fiber diet in managing primary open-angle glaucoma. Blumberg et al[13] identified elevated IOP as the most critical risk factor for glaucoma. Gillmann[14] and team delves into the immediate effects of everyday activities, such as emotional stress and

Table 1 Summary of Included Studies

	Authors	Summary
1.	**Rivera et al**[8]	The paper reviews important risk factors for the progression of primary open-angle glaucoma and emphasizes the need for further research to better understand and help patients at risk of progression and blindness.
2.	**Kumar et al**[9]	The paper discusses the current management of glaucoma focusing on Intra-Ocular Pressure reduction through pharmacological and surgical therapy, as well as the potential roles of lifestyle factors such as aerobic exercise, mindfulness, caffeine, and nicotinamide supplementation in lowering Intra-Ocular Pressure, offering neuroprotection, and slowing disease progression in individuals with open-angle glaucoma. Further research is needed to understand the long-term effects and mechanisms of these lifestyle factors in glaucoma management.
3.	**Leske et al**[10]	The paper discusses factors influencing glaucoma progression, the effects of treatment, and the benefits of Intra-Ocular Pressure reduction in reducing progression risk, providing valuable guidance for patient care and management.
4.	**Perez et al**[11]	The paper discusses the importance of environmentally modifiable factors in preventing or slowing the progression of glaucoma, such as lifestyle, exercise, and nutrition, and emphasizes the need for further research to confirm these findings.
5.	**Hecht et al**[12]	The paper discusses the impact of lifestyle factors on the management of primary open angle glaucoma, highlighting the potential benefits of moderate aerobic exercise and a high fiber diet rich in fruits and vegetables, while emphasizing the need for further research to establish stronger evidence-based recommendations.
6.	**Blumberg et al**[13]	Glaucoma is a multifactorial disease with various risk factors, but elevated Intra-Ocular Pressure stands out as the most crucial factor, impacting disease onset and progression significantly. The lamina cribrosa is identified as a key location for damage in glaucomatous optic neuropathy.
7.	**Gillmann et al**[14]	The paper evaluates the direct effect of common daily activities, such as emotional stress and resistance training, on intraocular pressure profiles in open-angle glaucoma and glaucoma suspect patients.
8.	**Dziedziak et al**[15]	This paper summarizes the evidence on the potential benefits of dietary antioxidants in preventing and treating the neurodegenerative ophthalmic diseases of age-related macular degeneration and glaucoma.
9.	**Yang et al**[16]	This large-scale population-based study in China found that long-term exposure to ambient fine particulate matter (PM2.5) was associated with increased odds of glaucoma, especially primary angle-closure glaucoma, and that middle-aged adults and non-smokers were more susceptible to the effects of PM2.5 on glaucoma risk.
10.	**Al Owaifeer et al**[17]	This paper reviews the current evidence on the role of diet, including obesity, dietary components, and supplements, in influencing intraocular pressure, the incidence of glaucoma, and the progression of the disease.
11.	**Tribble et al**[18]	The paper discusses how glaucoma is a leading cause of vision loss due to progressive retinal ganglion cell dysfunction and death, suggests that metabolic deficiencies and defects may play an important role in glaucoma pathophysiology, and states that modifying diet and exercise can be implemented by patients as an adjunct to intraocular pressure lowering, which may be beneficial for retinal ganglion cells in glaucoma.

Abbreviation: IOP: Intraocular pressure.

resistance training exercises, on intraocular pressure profiles in patients diagnosed with open-angle glaucoma and individuals suspected of having the condition. The study evaluates how these common activities might influence IOP levels. Meanwhile, Dziedziak et al[15] provided a review of the existing evidence on the potential benefits of dietary antioxidants in preventing and treating two age-related neurodegenerative ophthalmic diseases: age-related macular degeneration and glaucoma. The authors discuss the possible role of antioxidants in mitigating these conditions. Interestingly, Yang et al[16] in their large-scale, population-based study conducted in China investigated the association between long-term exposure to ambient fine particulate matter (PM2.5) and the risk of developing glaucoma. The findings revealed a link between PM2.5 exposure and an increased likelihood of glaucoma, particularly primary angle-closure glaucoma. The study also identified middle-aged adults and non-smokers as being more susceptible to the detrimental effects of PM2.5 on glaucoma risk. Adi et al[17] provided a review of the current evidence on the role of diet in

influencing various aspects of glaucoma, encompassing obesity, dietary components, and the use of supplements. The authors discuss how these dietary factors might influence IOP, the incidence of glaucoma, and the progression of the disease. Tribble et al[18] highlighted glaucoma as a leading cause of vision loss due to progressive dysfunction and death of retinal ganglion cells. The authors propose that metabolic deficiencies and defects might play a significant role in the pathophysiology of glaucoma. The study suggests that modifying diet and exercise habits could be implemented by patients as an adjunct to traditional IOP-lowering therapies. These lifestyle changes might offer potential benefits for protecting retinal ganglion cells in glaucoma.

Table 2 summarizes research on primary open-angle glaucoma, highlighting the importance of intraocular pressure (IOP) as a modifiable risk factor for glaucoma progression. Lifestyle modifications like aerobic exercise, mindfulness,

Table 2 Main Findings and Study Objectives

No.	Study	Main Findings	Study Objectives
1.	**Rivera et al**[8]	Intraocular Pressure (IOP): A major risk factor for glaucoma progression.	To review recent literature to identify possible risk factors leading to primary open angle glaucoma progression and blindness.
		Other contributing factors: Structural, vascular, and genetic factors also play a role.	
		Importance of understanding: Understanding these factors is crucial for improving glaucoma patient care and prevention.	
2.	**Kumar et al**[9]	Aerobic exercise: May be associated with neuroprotection and decreased disease progression in glaucoma patients.	The study objectives are to evaluate the roles of lifestyle factors in lowering Intraocular Pressure, offering neuroprotection, and/or slowing disease progression in individuals with open-angle glaucoma, and to review the literature on modifiable lifestyle factors in individuals diagnosed with open-angle glaucoma.
		Mindfulness exercises: May be associated with lower intraocular pressure (IOP) and neuroprotection in individuals with open-angle glaucoma.	
		Nicotinamide supplementation: Is linked to neuroprotection and short-term visual function improvement.	
3.	**Leske et al**[10]	Treatment effectiveness: Treatment halved the progression risk in glaucoma patients.	The study objectives are to assess factors for progression in the Early Manifest Glaucoma Trial (EMGT), including the effect of EMGT treatment.
		Initial Intraocular Pressure reduction: Lowering Intraocular Pressure at the beginning of treatment significantly influenced the outcome.	
		Risk factors for progression: Factors like higher baseline Intraocular Pressure, exfoliation, bilateral disease, worse mean deviation, older age, and frequent disc hemorrhages were associated with increased progression risk.	
4.	**Perez et al**[11]	Lifestyle modifications may be protective: Smoking cessation, moderate aerobic exercise, weight management, and a balanced diet may help prevent glaucoma or its progression.	The study objectives are to summarize the current evidence on environmentally modifiable factors such as lifestyle, exercise, and nutrition in the pathogenesis of glaucoma.
		Need for further research: More studies are needed to confirm these findings and establish a stronger causal relationship.	

(*Continued*)

Table 2 (Continued).

No.	Study	Main Findings	Study Objectives
5.	**Hecht et al**[12]	Certain lifestyle habits may influence glaucoma progression: While more research is needed, some evidence suggests that lifestyle factors could impact the disease.	The study objectives include reviewing the literature on modifiable lifestyle interventions in the management of primary open angle glaucoma, exploring the evidence on the relationship between environmental factors, behaviors, diet, and glaucoma, providing clarity on lifestyle and diet recommendations, contributing to the understanding of modifiable lifestyle interventions, and addressing the lack of guidelines on lifestyle advice for patients with primary open angle glaucoma.
		Sleeping position: Sleeping with the head elevated and avoiding the worst eye-dependent side may slightly lower intraocular pressure.	
		Food supplements and exercise: Some food supplements and moderate aerobic exercise may also help reduce Intraocular Pressure.	
6.	**Blumberg et al**[13]	Risk factors for open-angle glaucoma: older age, lower ocular perfusion pressure, African or Latino ancestry, elevated Intraocular Pressure, splinter hemorrhages, thinner central cornea, beta-zone parapapillary atrophy, and exfoliation syndrome are all associated with increased risk.	The study objectives are to identify ocular and systemic risk factors for glaucoma onset and progression and to review both known and novel risk factors for improved disease detection and management.
		Elevated IOP: Intraocular Pressure is the most critical risk factor for glaucoma development and progression.	
		Central corneal thickness (CCT): A strong predictor of glaucoma development.	
7.	**Gillmann et al**[14]	Emotional stress and resistance training: These activities were associated with a persistent elevation of intraocular pressure (IOP).	The main objectives of the study were to evaluate the direct effect of common daily activities, such as walking/cycling, resistance training, yoga/meditation, emotional stress, and alcohol consumption, on intraocular pressure (IOP)-related profiles.
		Walking/cycling: While causing a small increase in IOP during the activity, the effect was not sustained.	
		Yoga/meditation: These practices may have a potential benefit in lowering IOP, but more research is needed to confirm a statistically significant effect.	
8.	**Dziedziak et al**[15]	Dietary antioxidants: Resveratrol, carotenoids, and coenzyme Q10 may help prevent retinal cell neurodegeneration in AMD and glaucoma.	To review the current knowledge on dietary antioxidants that may play a role in diminishing oxidative stress and damage to retinal cells - To focus on age-related macular degeneration (AMD) and glaucoma, which are the two main neurodegenerative ophthalmic diseases in developed countries where oxidative stress is a key factor
		Need for new treatments: There's a growing need for more effective treatments for these diseases, especially dry AMD and glaucoma.	
		Safety and convenience: Dietary antioxidants are generally safe and convenient to use.	
		Mediterranean and Oriental diets: Diets rich in antioxidants have been linked to lower prevalence and progression of AMD.	

(*Continued*)

Table 2 (Continued).

No.	Study	Main Findings	Study Objectives
9.	**Yang et al**[16]	Long-term PM2.5 exposure: Associated with increased risk of glaucoma, especially primary angle-closure glaucoma (PACG).	The study objectives are: 1) To investigate the association between long-term PM2.5 exposure and odds of glaucoma, using satellite-based estimates of PM2.5 levels and nationwide survey data; 2) To identify individuals susceptible to PM2.5 exposure and glaucoma among Chinese adults, given the wide concentration gradient of PM2.5 pollution.
		Age susceptibility: Middle-aged adults (40–65 years old) are more susceptible to PM2.5's effects on glaucoma than the elderly.	
		Smoking impact: Non-smokers are more strongly affected by PM2.5 exposure on glaucoma risk compared to smokers.	
10.	**Al Owaifeer et al**[17]	PM2.5 exposure: Long-term exposure to PM2.5 (fine particulate matter) is associated with an increased risk of glaucoma, particularly primary angle-closure glaucoma (PACG).	The objective of the study was to provide a summary of the current evidence regarding the effect of obesity and diet on intraocular pressure, incidence, and progression of glaucoma.
		Age susceptibility: Middle-aged adults (40–65 years old) are more vulnerable to the harmful effects of PM2.5 exposure on glaucoma risk compared to the elderly.	
		Smoking impact: Non-smokers are more susceptible to the negative effects of PM2.5 exposure on glaucoma risk than smokers.	
11.	**Tribble et al**[18]	Glaucoma: A leading cause of irreversible vision loss due to retinal ganglion cell damage.	To summarize metabolism-modulating approaches, including diet and exercise that have been studied in the last 15 years for their potential neuroprotective and neurorecovery effects in glaucoma. To comment on the applicability of these metabolism-modulating approaches for neuroprotection and neurorecovery in glaucoma.
		Metabolic factors: Metabolic deficiencies and defects may contribute to glaucoma development.	
		Dietary and exercise interventions: Exercise, nicotinamide supplementation, pyruvate supplementation, and ketogenic diets may have neuroprotective effects in glaucoma.	

Abbreviation: IOP: Intraocular pressure.

and nicotinamide supplementation can slow disease progression. Treatment significantly reduces glaucoma progression risk, with initial IOP reduction crucial. Lifestyle changes like smoking cessation and a balanced diet may protect against glaucoma. Interventions like head elevation during sleep and moderate exercise can improve glaucoma progression. Risk factors include older age, lower ocular perfusion pressure, and central corneal thickness.

Table 3 presents a summary of studies on primary open-angle glaucoma (POAG), focusing on various methodologies and interventions. Key factors identified include intraocular pressure fluctuations and central corneal thickness (CCT). Lifestyle factors like aerobic exercise and mindfulness may lower IOP and provide neuroprotection. Treatments like argon laser trabeculoplasty reduced POAG progression risk. Lifestyle modifications like smoking cessation and balanced diets were also emphasized. Randomized controlled trials on food supplements and lifestyle changes also examined their effects on IOP. The studies emphasize the importance of managing IOP and identifying risk factors for POAG progression.

Table 4 presents limitations and future research directions for glaucoma studies. Rivera et al[8] suggest long-term studies to understand risk factors for disease progression and blindness, while Anika et al[9] in their study highlighted inconsistencies in evidence on lifestyle factors. Leske et al[19] in their study emphasized the variability in intraocular pressure measurements and the need for more data to distinguish risk groups. Perez et al[11] suggested large-scale

Table 3 Study Design, Methodology, Interventions, and Outcomes

	Authors	Study Design	Methodology	Intervention	Outcome Measured	Intervention Effects
1.	**Rivera et al**[8]	Observational study	Reviewed existing literature to identify risk factors for primary open-angle glaucoma progression and blindness. **Emphasis**: Need for long-term studies to better understand the disease.	The treatment approach was based on the anticipated disease progression. **Key factors considered**: Intraocular pressure (IOP) management, central corneal thickness monitoring, structural factors, vascular factors, and genetic factors were all considered.	The study aimed to understand factors influencing primary open-angle glaucoma progression and its impact on vision. It focused on measuring disease progression, identifying risk factors, and exploring their relationships. This helps in understanding glaucoma's complexity and developing effective prevention and treatment strategies.	Intraocular pressure (IOP) fluctuation may be a risk factor for glaucoma progression, but its exact role is unclear. Other factors like central corneal thickness, structural factors, vascular factors, and genetics also contribute to glaucoma development and progression.
2.	**Kumar et al**[9]	–	The study reviewed preclinical animal model studies and translated their findings to clinical populations to evaluate the effects of lifestyle factors on glaucoma. The authors emphasized the need for further research to confirm these findings over longer follow-up durations.	Aerobic exercise, mindfulness, caffeine, and nicotinamide supplementation	Lowering IOP, offering neuroprotection, slowing disease progression, short-term visual function improvement with nicotinamide supplementation	Aerobic exercise, mindfulness, and potentially nicotinamide supplements may benefit glaucoma patients by reducing disease progression, lowering IOP, and offering neuroprotection. Further research is needed to confirm the long-term effects of these interventions.
3.	**Leske et al**[10]	Randomized controlled trial, Longitudinal study, Analytical observational study	The study used statistical models to evaluate patient-based progression risk, using standardized criteria for visual field testing and optic disc assessment. Perimetric criteria were defined as significant changes in specific visual field points.	Argon laser trabeculoplasty, Topical betaxolol, Follow-up every 3 months	Progression measured by perimetric and photographic optic disc criteria; Progression risk; IOP reduction	Early treatment and addressing risk factors like higher baseline IOP, exfoliation, and bilateral disease are crucial for improving glaucoma outcomes. These factors, along with initial IOP reduction, significantly influence disease progression.

4.	**Perez et al**[11]	Observational study with large prospective studies, case-control studies, secondary analysis of data from a randomized control trial, and population-based studies	The methodology includes the mention of the need for large prospective studies, investigation of anthropometric parameters, dietary consumption associations, and a randomized controlled trial.	The study suggests that lifestyle modifications, including smoking cessation, aerobic exercise, weight management, and a balanced diet rich in specific nutrients, may be protective against glaucoma or its progression.	Caffeine intake, dietary consumption of specific fatty acids, supplemental vitamin C intake, effects of oral antioxidants on ocular blood flow	Aerobic exercise can lower IOP, while isometric exercise may temporarily raise it. Maintaining a healthy weight and diet may protect against glaucoma, with hot tea and omega-3 fatty acids potentially offering benefits. Observational studies can provide hypotheses about glaucoma risk factors.
5.	**Hecht et al**[12]	Randomized controlled trials with different food supplementation options in the management of POAG	The study used a systematic review approach to identify and evaluate relevant research on lifestyle interventions for primary open-angle glaucoma (POAG).	The study investigated the effects of various food supplements, lifestyle modifications, and avoidance of certain activities on glaucoma progression.	Intraocular pressure reduction, association between coffee intake and disease progression, potential negative effects of weight-lifting and yoga exercises	The study found that certain interventions, such as sleeping with the head elevated, food supplementation, exercise, and avoiding certain activities like yoga headstands and swimming goggles, can influence intraocular pressure (IOP). Some interventions, like food supplementation and exercise, were associated with a decrease in IOP, while others, like swimming goggles, may increase IOP.
6.	**Blumberg et al**[13]	Review Article	Literature Review	Not Applicable	Intraocular pressure (IOP), central corneal thickness (CCT), corneal hysteresis (CH), presence of splinter hemorrhages of the optic disc, and structural changes in the lamina cribrosa (LC)	Not Applicable

(*Continued*)

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Table 3 (Continued).

	Authors	Study Design	Methodology	Intervention	Outcome Measured	Intervention Effects
7.	**Gillmann et al**[14]	The study design was a prospective, non-controlled, observational study with a parallel design, conducted at a single site (University of California San Diego).	The study used a contact lens sensor to continuously monitor IOP-related variations in patients over 24 hours. Other measurements included central corneal thickness, keratometry, and Goldmann applanation tonometry. Patients recorded their daily activities, and CLS recordings with less than 80% valid measurements were excluded. The study compared IOP fluctuations during and after events to a baseline reference.	Participants received the SENSIMED Triggerfish contact lens sensor (CLS) to continuously monitor their intraocular pressure (IOP) related variations during their usual daily activities for 24 hours.	IOP-related profiles, measured in millivolt (mV) equivalents	The study found that walking/cycling, resistance training, and emotional stress were associated with elevated intraocular pressure (IOP). Yoga/meditation showed a potential, but not statistically significant, decrease in IOP. Alcohol consumption was linked to a temporary reduction in IOP.
8.	**Dziedziak et al**[15]	The paper is a review article, not a primary study, so it does not have a specific study design.	Not applicable (the paper is a review and does not describe a specific methodology)	The study participants received dietary supplements of zinc, resveratrol, carotenoids, coenzyme Q10, alpha-lipoic acid, and hesperidin. However, the specific dosages, frequencies, and durations of these interventions varied across the studies.	The effect of dietary antioxidants on diminishing oxidative stress and damage to retinal cells in AMD and glaucoma	Dietary supplements like zinc, resveratrol, carotenoids, coenzyme Q10, and alpha-lipoic acid have shown potential neuroprotective effects in animal models and clinical studies for both AMD and glaucoma. These supplements may help prevent retinal cell damage and reduce oxidative stress, which are key factors in these diseases.
9.	**Yang et al**[16]	The study design is a nation-wide, cross-sectional observational study using a multistage stratified cluster sampling procedure to enroll a nationally representative sample of rural Chinese adults, with the aim of investigating the regional distributions and risk factors for the epidemic of glaucoma.	The study used a multi-stage stratified cluster sampling procedure to recruit a nationally representative sample of rural Chinese participants. Participants underwent eye examinations, and PM2.5 exposure was estimated using a satellite-based model.	Not applicable (this is an observational study with no intervention)	The association between long-term exposure to ambient fine particulate matter (PM2.5) and glaucoma, including the subtypes of primary angle-closure glaucoma (PACG) and primary open-angle glaucoma (POAG)	The study found that long-term exposure to PM2.5 was associated with an increased risk of glaucoma, particularly primary angle-closure glaucoma (PACG). The risk of glaucoma increased by 7% for every 10 μg/m3 increase in PM2.5 exposure.

10.	**Al Owaifeer et al**[17]	This is a literature review paper.	The authors conducted a literature review using PubMed to identify studies on the relationship between diet, nutrition, and glaucoma. They focused on epidemiological and clinical studies published in English between 1966 and 2017.	The study investigated the effects of dietary supplements like ginkgo biloba and saffron on glaucoma. Ginkgo biloba was found to improve retinal blood flow and visual function in normal tension glaucoma, while saffron was shown to reduce intraocular pressure in primary open-angle glaucoma.	Not mentioned (the paper is a review and does not report on a specific study with a primary outcome)	Ginkgo biloba extract has been shown to improve retinal blood flow and visual function in normal tension glaucoma patients. Saffron has been found to reduce intraocular pressure in patients with primary open-angle glaucoma.
11.	**Tribble et al**[18]	Not mentioned (the paper is a review and does not describe a specific study design)	Not applicable (the paper is a review and does not describe a specific methodology)	Nicotinamide supplementation at ~2.5 g/day, long-term oral pyruvate supplementation, and a ketogenic diet	Retinal ganglion cell function and survival, optic nerve/axon degeneration, and visual function (eg visual field, contrast sensitivity)	Not applicable (the paper is a review and does not describe a specific methodology)

Abbreviation: IOP: Intraocular pressure.

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Table 4 Limitations and Future Research Directions

S. No.	Authors	Limitations	Future Research
1.	**Rivera et al**[8]	The study highlights the need for further research to understand glaucoma progression, interpret factors, apply genetic findings, and understand risk factors.	Conducting prospective long-term studies to identify risk factors for POAG progression, understand the factors leading to visual impairment, and predict vision and quality of life outcomes for tailored treatment to prevent blindness.
2.	**Kumar et al**[9]	The study highlights the need for further research to incorporate lifestyle factors into standard clinical practice. Preclinical studies can help elucidate underlying mechanisms, while clinical studies with additional endpoints and longer follow-up can strengthen our understanding of lifestyle factors in glaucoma.	Future research should assess lifestyle factors in preclinical experimental models and clinical glaucoma populations over the long-term to enhance understanding of the mechanisms underlying associated clinical recommendations.
3.	**Leske et al**[10]	- Inherent variation in IOP measurement - Caution needed when applying study results to individual patients - Need for additional data to distinguish risk groups - Anticipation of further publications by investigators	The study highlights the need for further research to distinguish different risk groups for glaucoma progression and to gain a better understanding of treatment strategies and expected outcomes for glaucoma patients.
4.	**Perez et al**[11]	Lack of large prospective or randomized controlled trials with long follow-up - Difficulty in establishing cause-effect relationships - Need for further investigation to prove associations - Difficulty in drawing important clinical correlations (due to limited study designs)	Future research should focus on conducting large prospective studies with long-term follow-up to confirm the impact of lifestyle habits, exercise, and nutrition on glaucoma progression. Additionally, research is needed to evaluate the effects of specific dietary components on glaucoma risk.
5.	**Hecht et al**[12]	Retrospective nature of the evidence - Limited amount of randomized controlled trials - Difficulty in drawing clinical correlations - Need for future studies and randomized controlled trials to test clinical correlations and examine the effects of MLS on POAG patients	The study emphasizes the need for more randomized controlled trials to investigate the effects of modifiable lifestyle interventions on primary open angle glaucoma patients. These studies should aim to provide robust evidence on the impact of behaviors, environmental factors, and diet on intraocular pressure and disease progression.
6.	**Blumberg et al**[13]	-	Investigating the role of cerebrospinal fluid pressure in glaucoma development and progression, particularly in different subtypes of glaucoma such as normal-tension glaucoma and ocular hypertension.
7.	**Gillmann et al**[14]	Small sample size, with only 41 eyes and even fewer patients partaking in each activity - Reliance on non-standardized self-reported activities, which introduces bias from not controlling for confounding factors	The study emphasizes the need for further research to explore the effects of more day-to-day events on IOP and to confirm the specific factors influencing these variations. Additional research is also needed to confirm the findings on the association between emotional stress, resistance training, and IOP, as well as to assess the effect of glaucoma surgery on IOP fluctuations.

(*Continued*)

Table 4 (Continued).

S. No.	Authors	Limitations	Future Research
8.	**Dziedziak et al**[15]	- Inconsistent outcomes of clinical trials, especially for vitamins and omega-3 fatty acids in glaucoma and AMD - Need for larger, more properly planned clinical studies - Lack of clinical studies on the role of alpha-lipoic acid, resveratrol and hesperidin in glaucoma, and resveratrol in AMD, despite promising effects shown in animal models and case series	The study emphasizes the need for larger, well-planned clinical trials to investigate the role of vitamins and omega-3 fatty acids in AMD and glaucoma. Additionally, further research is needed to study the effects of alpha-lipoic acid, resveratrol, and hesperidin in glaucoma and resveratrol in AMD.
9.	**Yang et al**[16]	The study was observational, limiting its ability to establish causality. Other limitations include small sample size, lack of data on indoor air pollution and time-activity patterns, and not considering co-exposure effects of other pollutants. The smoking data was limited, and a substantial number of participants were excluded due to missing data.	Future research should use a prospective study design with more accumulated cases of glaucoma to investigate the differential effects of PM2.5 exposure on PACG and POAG. Additionally, research should explore the specific biological mechanisms linking PM2.5 exposure and glaucoma risk.
10.	**Al Owaifeer et al**[17]	- The majority of results are from observational studies, rather than randomized controlled trials - Well-designed, randomized, controlled, clinical trials are required to reinforce the current body of evidence	Well-designed, randomized, controlled, clinical trials are required to reinforce the current body of evidence on the role of diet in glaucoma.
11.	**Tribble et al**[18]	- Self-reported glaucoma incidence, though offset by large cohort size and dose-dependent outcomes - Poor adherence and tolerability of ketogenic diets in humans - Difficulty in controlling for and separating effects of caloric intake in ketogenic diet studies - Need for clinical trials using controlled ketogenic or derivative diets to assess effects on glaucoma	The authors recommend future research on ketogenic diets, ketone bodies, pyruvate, and nicotinamide supplementation to assess their potential neuroprotective effects in glaucoma.

prospective or randomized controlled trials to confirm lifestyle habits and dietary components' impact on glaucoma. Hecht et al[7] emphasize the retrospective nature of current research and the importance of investigating cerebrospinal fluid pressure in different glaucoma subtypes.

Discussion

Glaucoma is a leading cause of irreversible vision loss worldwide. It is characterized by the progressive degeneration of retinal ganglion cells (RGCs) and their axons, ultimately resulting in visual field loss. While intraocular pressure (IOP) remains a well-established risk factor for glaucoma progression, recent research indicates that environmental and lifestyle factors may also significantly influence disease development and progression. The aim of this systematic review was to assess the current body of evidence regarding the impact of environmental factors on glaucoma progression.

Our review identified several key findings that support and expand upon existing research. First, we confirm that IOP is the most critical modifiable risk factor for glaucoma progression. This conclusion is consistent across multiple studies, including the Early Manifest Glaucoma Trial (EMGT),[19] which demonstrated that effective treatment significantly reduces progression risk by half (The EMGT Group, 2000). Additionally, our analysis underscores the potential benefits of lifestyle modifications in lowering IOP and potentially slowing disease progression. Previous research has linked aerobic exercise to reduced IOP and slower rates of visual field deterioration in glaucoma patients.[20] Furthermore, our review explores the potential neuroprotective effects of mindfulness practices, suggesting a promising area for future investigation into non-traditional glaucoma management interventions. While using nicotinamide supplements in glaucoma warrants further study, our findings align with preclinical research suggesting their potential neuroprotective properties.[21]

Our review also highlights the emerging connection between environmental pollution and glaucoma. The positive correlation we observed between long-term exposure to PM2.5, a significant component of air pollution, and glaucoma risk aligns with recent findings by Chiang et al.[22] Their study similarly linked PM2.5 exposure to an increased risk of primary open-angle glaucoma (POAG) in a large Chinese population. Further research is essential to elucidate the mechanisms through which air pollution contributes to glaucoma development. Potential mechanisms include oxidative stress induced by air pollutants, leading to damage of RGCs, or inflammatory responses triggered by airborne particles.[23] Investigating these pathways can provide valuable insights into the causal relationship between environmental pollution and glaucoma.

Our findings also underscore the susceptibility of specific populations to environmental risk factors. For instance, our review suggests that middle-aged adults and non-smokers may be more vulnerable to the effects of PM2.5 exposure on glaucoma risk. This susceptibility could be linked to age-related variations in blood–brain barrier function or individual differences in detoxification pathways that affect susceptibility to environmental toxins.[24] Additionally, our review highlights the potential protective role of a balanced diet rich in specific nutrients against glaucoma. This aligns with previous research indicating the benefits of dietary antioxidants such as lutein and zeaxanthin in reducing oxidative stress and protecting retinal cells.[25]

Limitations of our review include the predominantly observational nature of the included studies, which complicates establishing definitive cause-and-effect relationships between environmental factors and glaucoma progression. Moreover, the variability in methodologies and interventions across studies limits our ability to draw definitive conclusions. Future research should prioritize well-designed prospective studies to investigate the causal relationships between environmental exposures and glaucoma. Additionally, future studies need to explore the biological mechanisms through which environmental factors contribute to glaucoma development. Furthermore, randomized controlled trials are essential to assess the effectiveness of specific lifestyle modifications, dietary interventions, or environmental mitigation strategies in preventing or slowing glaucoma progression.

Challenges and Ethical Considerations

While our review suggests promise for environmental modifications as potential glaucoma management strategies, implementing these changes can be challenging. For instance, air quality control measures often require significant infrastructure investments and policy changes, posing limitations in areas with limited resources. Additionally, individual efforts to reduce exposure to air pollution may be limited by factors such as dependence on private transportation or living in areas with high levels of industrial activity.

Ethical considerations also arise when discussing environmental interventions. Widespread pollution control strategies often require substantial financial resources. Striking a balance between environmental protection, economic development, and public health is crucial. Furthermore, the cost-effectiveness of implementing such strategies on a large scale needs to be carefully evaluated.

Conclusion

Our systematic review underscores the multifaceted nature of glaucoma, highlighting the interplay between established risk factors like intraocular pressure (IOP) and emerging environmental influences like air pollution. While the existing literature on environmental factors and glaucoma progression is rapidly evolving, our review offers several valuable contributions. Based on our findings, we recommend that clinicians consider incorporating environmental risk reduction strategies, such as reducing exposure to air pollution and promoting healthy lifestyle behaviors, into their glaucoma management plans. Future research should focus on elucidating the biological mechanisms through which environmental factors contribute to glaucoma development and progression, as well as evaluating the effectiveness of targeted interventions to address these factors.

Abbreviations

IOP, Intraocular Pressure; POAG, Primary Open-Angle Glaucoma; AMD, Age-Related Macular Degeneration; PM2.5, Fine Particulate Matter (with diameter 2.5 micrometres or less); RCT, Randomized Controlled Trial; MLS, Modifiable Lifestyle Interventions; CSF, Cerebrospinal Fluid; RGCs, Retinal Ganglion Cells; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Data Sharing Statement

All relevant data are within the paper.

Author Contributions

Author is responsible for conception and design, acquisition of data, or analysis and interpretation of data; drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The author declares that they have no conflicts of interest in this work.

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