Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v30i16.2323

ASSOCIATION BETWEEN SLEEP APNEA AND GLAUCOMA: A SYSTEMATIC REVIEW

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Abstract:
There has been an ongoing debate in the literature as to whether sleep apnea is associated with glaucoma. While certain studies have established a link between sleep apnea and normal- tension glaucoma (NTG) and/or open-angle glaucoma (OAG), other studies have found no such association. To address this issue, we conducted a systematic review to determine whetherthere is a significant positive correlation between obstructive sleep apnea syndrome (OSAS) and the prevalence of glaucoma.

Methodology:
All studies including the association between Sleep Apnea and Glaucoma were included in the study. We only included studies that defined OSA (Obstructive Sleep Apnea) using the AHI (Apnea Hypopnea Index) via polysomnography or home sleep apnea testing (HSAT/polygraph). Additionally, we included studies that utilized at least one of the following ophthalmic examination techniques to assess glaucoma: measurement of intraocular pressure (IOP), optical coherence tomography (OCT) imaging, sonography, and perimetry for measuring the visual field (VF).

Result:
The study was conducted by PRISMA (Preferred Reporting Item for Systematic Review and Meta-Analysis) 2020 Checklist. This systematic review was conducted and reported according to Cochrane Handbook and PRISMA statement. The database PubMed, Scopus, and Embase was thoroughly searched, resulting in the retrieval of 2471 articles from various databases, and 6 additional articles were added through the snowballing method. Out of these, 1800 articles were eliminated due to duplicates. 677 articles were screened, and 39 were excluded because they were in languages other than English, leaving 638 articles for the title and abstract screening. Ultimately, 38 articles were included in the full-text screening.

Keywords: Sleep apnea, glaucoma, PRISMA, perimetry, sonography, optical, dentist

INTRODUCTION

Glaucoma is a type of eye disorder that can cause damage to the optic nerve, which is responsible for transmitting visual information from the eye to the brain. It is most commonly seen in individuals over the age of 40, and primary open-angle glaucoma is the most prevalent type.[1-3]
The initial stages of glaucoma are usually asymptomatic, which means that people may not realize that they have the condition until it has advanced. That's why it's crucial to have regular eye examinations, particularly for those at higher risk of developing glaucoma, such as people with a family history of the disease, individuals with diabetes, and those of African descent.[4,5] If left untreated, glaucoma can cause vision loss and even blindness in severe cases. However, with timely detection and appropriate treatment, it is possible to slow or halt the progression of the disease and preserve vision.[6-8] Depending on the severity of the condition, treatment options may include medications, laser therapy, or surgery.

Obstructive Sleep Apnea is understood as a disorder characterized by repetitive partial or complete obstruction of the upper airway during sleep, causing oxygen desaturation and becoming a risk factor for cardiovascular and neurological diseases.[9] The main symptoms are snoring, daytime sleepiness, difficulty in concentrating, and morning headache. Risk factors include obesity, gender, upper respiratory abnormalities, and consumption of alcohol.

Obstructive sleep apnea (OSA) has been identified in some population studies as a possible risk factor for glaucoma. Its prevalence has been estimated at 27% but varies in different epidemiological studies.[10-12]

There has been an ongoing debate in the literature as to whether sleep apnea is associated with glaucoma. While certain studies have established a link between sleep apnea and normal- tension glaucoma (NTG) and/or open-angle glaucoma (OAG), other studies have found no such association.[13,14] To address this issue, we conducted a systematic review to determine whether there is a significant positive correlation between obstructive sleep apnea syndrome (OSAS) and the prevalence of glaucoma.

METHODOLOGY

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Eligibility criteria Inclusion Criteria:

All studies including Association between Sleep Apnea and Glaucoma were included in the study. We only included studies that defined OSA (Obstructive Sleep Apnea) using the AHI (Apnea Hypopnea Index) via polysomnography or home sleep apnea testing(HSAT/polygraphy). Additionally, we included studies that utilized at least one of the following ophthalmic examination techniques to assess glaucoma: measurement of intraocular pressure
(IOP), optical coherence tomography (OCT) imaging, sonography, and perimetry for measuringthe visual field (VF). Articles published in the English Language were selected.

Exclusion Criteria:

Any grey literature including letters to the editor, and conference proceedings.

Information sources:

A systematic review was performed on PubMed, Scopus, Web of Science, and LILACS for articles

in the English language between 27.2.23- 12.3.23. The publication was searched both online and offline.

Search Strategy:
MeSH terms were used for glaucoma and sleep apnea, whereas synonyms were also found. Boolean operators “AND” “OR” and “NOT” were used with these terms for searching the articles. The following search terms were used adding a filter for age above 18 years. A manual search was also conducted. The full text was retrieved for all authors and was independently reviewed by all authors.

sleep apnea: "sleep apnea"[All Fields] OR "sleep apnea syndromes"[MeSH Terms] OR ("sleep"[All Fields] AND "apnea"[All Fields] AND "syndromes"[All Fields]) OR "sleep apnea syndromes"[All Fields] OR ("sleep"[All Fields] AND "apnea"[All Fields]) OR "sleep apnea"[All Fields]

For Scopus “Sleep Apnea??” “ ?” Glaucoma??” “Sleep Apnea PRE/0 ” and “Glaucoma PRE/0 was used.

Selection process:
Study selection:
The eligibility of identified studies was reviewed sequentially by one author for title, abstract, and full text against the eligibility criteria, and then separately by a second author, with any discrepancies handled by a third author.
Review articles, Case series, Case Reports and letters to the editor were excluded.

Types of Participants:
Patients above the age of 18 years with glaucoma and sleep apnea were included.

Data Extraction:
Authors independently gathered study features and numerical data from included studies using: The data collected for cross-sectional and case-control studies included the author's name, publication year, country of origin, study design, participant selection process, age range, glaucoma type(s), the total number of cases and controls, a diagnostic method for glaucoma, the method used to assess obstructive sleep apnea syndrome (OSAS), covariate adjustments made, and the authors' conclusions.

For cohort studies, the follow-up period was also recorded.

Data were extracted by two reviewers and entered into an Excel sheet. In case of any disagreement, it was resolved by the third reviewer, an expert in the field.

Data collection and items included:
For qualitative analysis general characteristics, the intervention involved and outcomes were assessed in each study in the form of author, year of the study conducted, study design, participant’s age, and gender distribution.

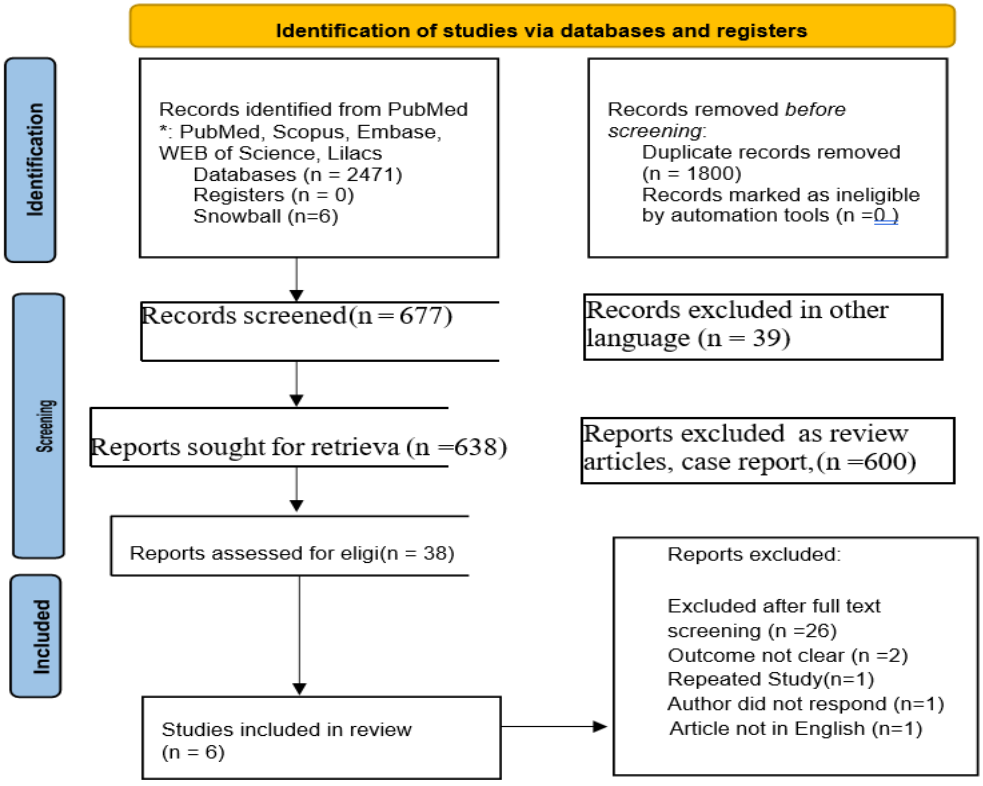
Study Selection:
Observational studies and randomized controlled trials were included in the study which include an association between glaucoma and Sleep Apnea, Quality appraisal and calibration of risk of bias were performed by two independent reviewers following the STROBE (Strengthening the reporting of observational studies in epidemiology) statement.

Study risk of bias assessment:
ROBINS -E was used to assess the risk of bias.

RESULT

Study Selection:
The database was thoroughly searched, retrieving 2471 articles from various databases, and 6 additional articles were added through the snowballing method. Out of these, 1800 articles were eliminated due to duplicates. 677 articles were screened, and 39 were excluded because they were in languages other than English language, leaving 638 articles for the title and abstract screening. Ultimately, 38 articles were included in the full-text screening. Among the 38 articles, 26 were deemed irrelevant based on factors such as age, outcome parameters, and relevance, while 2 were eliminated due to unclear outcomes, 1 could not be obtained, and another was not in the English language. Additionally, 1 article was excluded because it was a repeated study. As a result, only 6 studies were selected for qualitative analysis,as shown in Figure 1 of the PRISMA flowchart.
All studies included were observational studies, 3 of them were cross-sectional, 2 were case-control and one was a retrospective cohort study.
The Age group of the study participants varied from 44-70 years. Study participants were from different parts of the world. 5 studies showed a correlation between Sleep apnea and glaucoma.

Risk of bias:
Risk of Bias showed low risk of bias for 4 studies. Some concern was seen in 2 studies.



RESULT:

Study ID	Location	Study design	Sample Size	Age	Result
Kathrina Bahr etal 2020 [8]	Germany	Cross-sectional	110	64.3	No Correlation
Sergi et al 2007	Milano	Cross-sectional	51		Significant association
Chuang et al. 2020 [9]	Taiwan	Retrospective	83	48-54 years	Significant correlation
Morsy et al. [10]		Cross-sectional Case-control study	100		Significant correlation
Ching et al 2013[11]		A retrospective, matched-cohort study.	7084		Our results suggest that OSA is associated with an increased

					risk of subsequent OAG diagnosis during a 5-year follow-up period.
Daniet et al 1999 [12]	Switzerland	Cross-sectional study.	114	NA	High prevalence

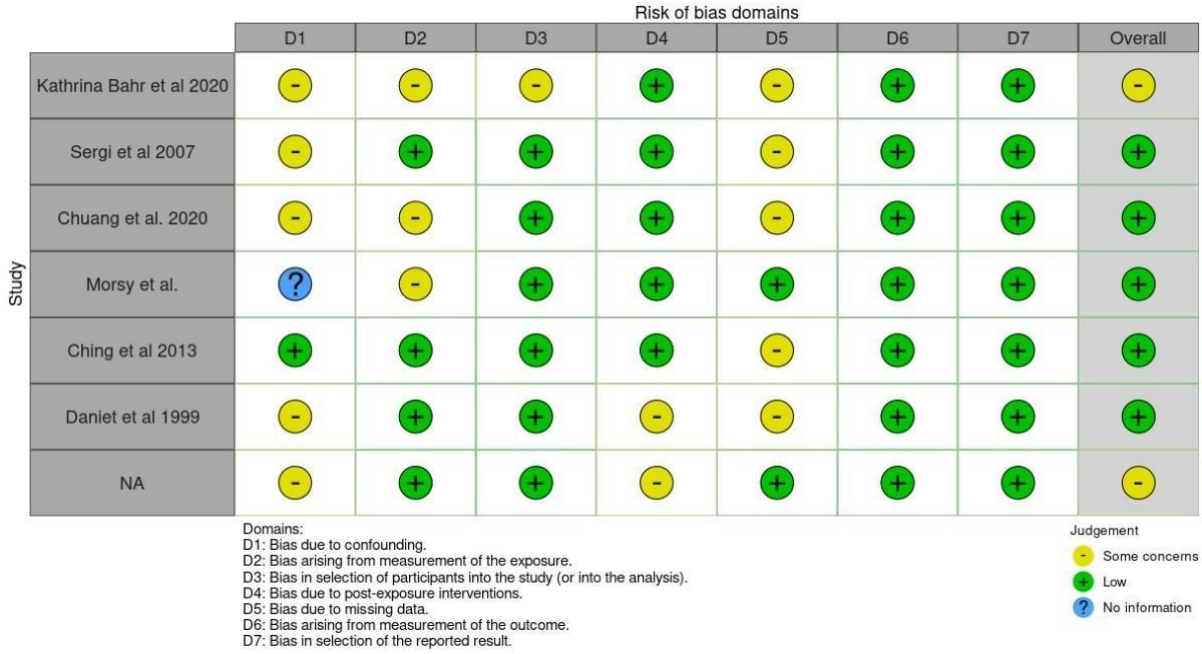


Figure 1: Risk of Bias Using Traffic Light Plot

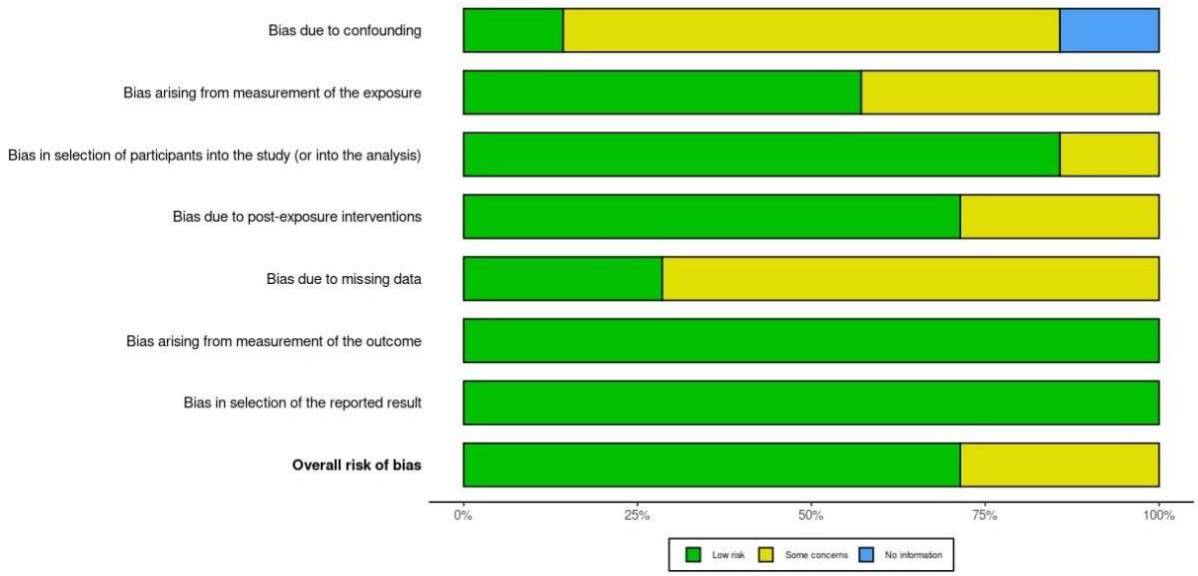


Figure 2: Overall Risk of Bias Using Traffic Light Plot

DISCUSSION:

The findings from our study suggest a connection between obstructive sleep apnea (OSA) and glaucoma. However, it is important to acknowledge that establishing a definite causal relationship between these two conditions is challenging due to the lack of prospective, randomized studies.

Our results are consistent with a meta-analysis conducted by Wu Koh et al. in 2015, which examined 12 studies involving 36,909 participants to explore the link between OSA and glaucoma risk.

In the meta-analysis, Wu Koh et al. observed that individuals with severe OSA had a significantly

higher risk of developing glaucoma (OR = 5.49; 95% CI) compared to those with mild or moderate OSA. This finding suggests a potential dose-response relationship, indicating that the severity of OSA may be associated with an increased risk of glaucoma. It is worth notingthat this observation strengthens the notion that OSA might play a role in the development or progression of glaucoma.[10] Furthermore, the meta-analysis by Wu Koh et al. revealed that OSA patients had an elevated riskof developing primary open-angle glaucoma (OR = 1.87; 95% CI). Primary open-angle glaucoma is the most common form of glaucoma and is characterized by elevated intraocular pressure. However, no significant association was found between OSA and normal-tension glaucoma (OR = 3.57; 95% CI), a type of glaucoma where intraocular pressure remains withinthe normal range. This suggests that the relationship between OSA and glaucoma may be specific to certain subtypes of the disease.[10,11]

International studies and various meta-analysis exhibit a brief relationship between sleep apneaand glaucoma such as SRMT done by Liu D, et a which provides a comprehensive analysis of the existing literature on the association between sleep apnea and glaucoma, further supporting the connection between these conditions.[12]

In a study compiled by Shinmei Y, et al. they investigated the association between glaucoma and sleep apnea in a Japanese population, providing insights into the relationship across different ethnic groups which was in conjunction with the current study.[13]

Studies conducted by Mojon, et al and Lin PW, Friedman M, Lin HC, et al. significantly associated the population-based matched-cohort studies which examined the significant association between glaucoma and sleep apnea, reinforcing the findings of the correlationbetween these conditions.[14,15]

In conclusion, our findings, along with the meta-analysis conducted by Wu Koh et al., suggest a potential association between OSA and glaucoma. However, further research is needed to elucidate the underlying mechanisms and establish a definitive causal relationship.

Understanding the link between OSA and glaucoma has important clinical implications, as it may guide screening, early detection, and management strategies for patients at risk. Continued investigation in this field is warranted to expand our knowledge and potentially improve the outcomes for individuals with OSA and glaucoma.

ROLE OF DENTISTS:

Dentists can contribute to the management of sleep apnea, a condition characterized byinterrupted breathing during sleep.[16,17]

They can provide assistance in the following ways:

Oral Appliance Therapy: Dentists can design and fit custom-made oral appliances, also known as mandibular advancement devices (MADs) or oral sleep appliances. These devices help keep the airway open by repositioning the jaw and tongue, reducing the chances of airway blockage during sleep.[18,19]

Collaboration with Sleep Specialists: Dentists often work in collaboration with sleep specialistsor physicians to diagnose and develop a treatment plan for sleep apnea patients. They can refer patients to specialists for comprehensive evaluations, sleep studies, and medical interventions if necessary.[20-23]

Continuous Monitoring: Dentists may incorporate technologies like home sleep apnea testing (HSAT) or portable sleep monitoring devices to assess the effectiveness of oral appliances andthe progress of sleep apnea treatment.[24]

Glaucoma is an eye condition that causes optic nerve damage and can lead to vision loss. Although dentists do not directly treat glaucoma, they can contribute to the management andearly detection of this condition in the following ways:

Routine Oral Examinations: During routine dental check-ups, dentists may observe signs ofpotential health issues, including changes in the eyes. They can detect certain ocular manifestations associated with glaucoma, such as changes in the optic nerve appearance, increased cup-to-disc ratio, or other visible abnormalities.[25,26]

Referral and Collaboration: If dentists suspect ocular abnormalities, they can refer patients to ophthalmologists or eye care specialists for further evaluation. Collaboration between dental andeye care professionals helps ensure comprehensive care and early detection of glaucoma.[27,28] Medicational Considerations: Dentists should be aware of patients' existing medications, including those used to treat glaucoma. Some glaucoma medications can cause dry mouth as a side effect, potentially impacting oral health.[29]

Dentists can consider these factors while developing treatment plans or prescribing medicationsthat may worsen dry mouth symptoms.

CONCLUSION

Sleep Apnea is considered a significant risk factor for the development of glaucoma, and several studies have established a strong association between the two conditions. For patients with Sleep Apnea, it is recommended that a comprehensive ophthalmic assessment should be performed at each follow-up visit. Glaucoma patients with obesity and progressive visual field damage, under low eye pressure (i.e., normal-tension glaucoma), should also be evaluated for Sleep Apnea and other sleep disorders.

LIMITATION:

The present study is not a meta-analysis, so the direct comparability of the included studies is not given, which is the main limitation. The limited number of studies and lack of a universal measurement scale across the studies make it difficult to compare the studies.

RECOMMENDATION:

More studies with standardized measurement tools will make it easy to measure the effect using quantitative analysis.

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