RESEARCH PAPER

Effect of Smoking on Macular Thickness and Visual Functions in Diabetes Mellitus: A PRISMA-Based Systematic Review

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ABSTRACT

Background: Diabetes mellitus is a major cause of retinal abnormalities and smoking may further affect retinal structural and functional changes. Advanced imaging modalities such as optical coherence tomography (OCT) and OCT angiography (OCTA) enable detailed evaluation of these changes.

Purpose: To systematically review the existing evidence on the impact of smoking on macular thickness and visual function in individuals with diabetes mellitus.

Methods: A systematic review was conducted following PRISMA 2020 guidelines. Electronic databases including PubMed, Scopus, Web of Science and Google Scholar were searched for studies published between 2010 and 2026. Studies involving diabetic participants with documented smoking exposure and reporting OCT-based macular parameters or visual function outcomes were included. Data extraction and study selection were performed independently.

Results: A total of 20 studies met the inclusion criteria. Diabetes mellitus was primarily associated with increased macular thickness and progressive retinal structural changes, particularly in the advanced stages of diabetic retinopathy. Smoking shows significant effects on retinal microvasculature, including reduced vessel density and thinning of retinal and choroidal layers. Some studies also reported early microvascular changes in diabetic smokers without clinically visible retinopathy. However, a few studies showed no significant structural changes, indicating variability across findings.

Conclusion: Both diabetes and smoking independently and jointly influence retinal morphology and function. Smoking may worse sub-clinical retinal damage in diabetic individuals, emphasizing the importance of early detection and smoking cessation. Further longitudinal studies are required to establish causal relationships.

Keywords: *Diabetes Mellitus, Smoking, Macular Thickness, Optical Coherence Tomography, Retinal Microvasculature, Visual Function.*

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INTRODUCTION

Diabetes mellitus (DM) represents a major global health burden, affecting over 450 million individuals in 2019 and projected to exceed 700 million by 2045. The rising prevalence, particularly in Asian countries like India, China etc., is further compounded by a high proportion of prediabetes. Diabetes mellitus, once considered a disease of older adults, is increasingly observed in younger populations. Early-onset DM is associated with a more aggressive metabolic profile, including rapid beta-cell dysfunction and increased insulin resistance (1). In terms of ocular scenario Diabetic Macular Edema (DME) is a leading cause of vision loss. In diabetic patients, primarily resulting from breakdown of the blood-retinal barrier and subsequent fluid accumulation in the macula. Structural OCT has become an essential, non-invasive tool for diagnosing and monitoring DME, enabling detailed visualization of retinal architecture. Advanced OCT analysis allows evaluation of key biomarkers such as Retinal Pigment Epithelium (RPE), and External Limiting Membrane (ELM) integrity which are closely associated with visual outcomes. These morphological features provide valuable insights for predicting disease progression and visual prognosis in DME (2). Along with this there are multiple other systemic events that can affect the ocular health of an individual, one among them is smoking. As per World Health Organization (WHO), smoking is the leading cause of mortality and morbidity around the world. Chronic smoking is a well-established risk factor for systemic diseases and has significant

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adverse effects on ocular health, including increased risk of macular degeneration, uveitis and vascular disorders. It affects both acute and chronic changes in the retinal and choroidal tissues, affecting thickness, perfusion and vascular integrity. Smoking-related vascular changes include arteriolar narrowing, increased stiffness and compromised blood flow.

Optical Coherence Tomography (OCT) as a non-invasive imaging modality, enables detailed assessment of retinal vascular density and choroidal thickness, aiding in the evaluation of these changes in smokers (3). Previous studies evaluating acute post-smoking effects have reported inconsistent findings, leaving the impact of smoking on retinal microvasculature unclear. OCT assessment in diabetic patients without clinically visible retinal changes provides a sensitive approach to detect early microvascular changes. Such changes may indicate an increased risk of progression to diabetic retinopathy or related diseases. Therefore, investigating smoking-related OCT vascular changes in this population is crucial for understanding early disease risk (4). Optical coherence tomography angiography (OCTA), an advanced extension of OCT, enables quantitative assessment of retinal and choroidal microvascular density. It has proven useful in detecting vascular changes, such as reduced peripapillary vessel density in various ocular conditions. Comprehensive ocular evaluation, including visual acuity, slit-lamp examination, intraocular pressure and OCTA, allows detailed assessment of ocular structure and perfusion.

Additionally, consideration of both active and passive smoking exposure is important when evaluating microvascular changes (5). Cigarette smoking significantly elevates the risk of both systemic and ocular vascular diseases. Although the exact mechanisms remain unclear, nicotine-induced peripheral vasoconstriction is thought to play a key role. This vasoconstriction increases vascular resistance, potentially compromising ocular blood flow. Such changes may contribute to the development of microvascular abnormalities in the eye (6). Even tobacco products contain thousands of chemicals, many of which are harmful and contribute to systemic diseases through microvascular and macro-vascular damage. These toxic substances are responsible for increased risks of cancer, cardiovascular and pulmonary conditions in both active and passive smokers. Such vascular changes can also impact ocular health and perfusion. OCTA, a non-invasive and repeatable imaging modality, enables detailed visualization of retinal and choroidal vasculature, facilitating the assessment of these smoking-induced microvascular changes (7). Macular thickness is an important parameter used in the diagnosis and monitoring of macular diseases. OCT has become a standard tool in clinical practice for evaluating macular pathology and assessing treatment outcomes (21).

A systematic review conducted under the PRISMA 2020 framework can help determine whether smoking independently affects macular thickness and retinal structural parameters in individuals with diabetes mellitus. It can also clarify the association between smoking and changes in visual functions, including best corrected visual acuity (BCVA) and contrast sensitivity. These insights are clinically important for guiding screening strategies and reinforcing smoking cessation in the management of diabetic patients. Given the clinical relevance-smoking is modifiable and macular integrity is critical for vision. There is a compelling need for a rigorous synthesis of available evidence. This systematic review aims to critically evaluate and synthesize existing evidence on the effects of cigarette smoking on macular thickness and visual function in individuals with diabetes mellitus. It focuses on findings derived from OCT-based imaging and psychophysical assessments.

METHODOLOGY:

To guarantee methodological rigor and transparency, this systematic review was carried out in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses-2020 (PRISMA 2020) guidelines. To reduce bias, two reviewers independently selected the studies and extracted the data. This method improves the validity and dependability of the review's conclusions. The inclusion and exclusion criteria were defined using the PECOS framework to ensure systematic selection of relevant studies. Studies involving diabetic participants with documented cigarette smoking exposure and appropriate non-smoking comparators were included. Primary outcomes focused on OCT-based macular thickness, while secondary outcomes included visual function measures such as BCVA and contrast sensitivity. Non-diabetic populations, non-comparable designs, and studies lacking quantitative outcomes were excluded to maintain methodological rigor.(9).

Relevant studies published between 2010 and 2026 in English were systematically identified through a comprehensive search of electronic databases including Google Scholar, PubMed, Scopus and Web of Science. The search strategy contained both controlled vocabulary (MeSH terms) i.e., *"diabetes mellitus", "smoking", "functional vision", "macular thickness"* and free-text keywords, tailored to each database and combined using Boolean operators to maximize retrieval of relevant literature. Additionally, reference lists of included articles and related reviews were manually screened to ensure no relevant studies were missed.

All retrieved studies were imported into Mendeley Desktop 1.19.8 for efficient management and duplicate removal. The screening process was conducted independently, beginning with titles and abstracts, followed by full-text assessment of potentially eligible studies based on predefined inclusion and exclusion criteria. A standardized data extraction method was used to ensure consistency and accuracy in the data collection. The overall study selection process was systematically documented using a PRISMA 2020 flow diagram, using the stages of identification, screening, eligibility and final inclusion (10). As shown in **Fig. 1**.

The PRISMA flow diagram shows how studies were selected for this systematic review in a step-by-step manner. A total 65 records were found from different databases like PubMed, Scopus, Web of Science and Google Scholar. After removing 5 duplicate records and 5 records by automatic tool, the remaining studies were screened by titles and abstracts. During this step, 8 studies were removed because they were not related to smoking or diabetes. Then, 37 full-text articles were searched, but 18 could not be obtained. So, 29 full-text studies were checked for eligibility. Out of these, 9 studies were excluded due to reasons like no proper comparison group, duplicate data or poor methodology. So, 20 studies met all the criteria and were included in this systematic review.

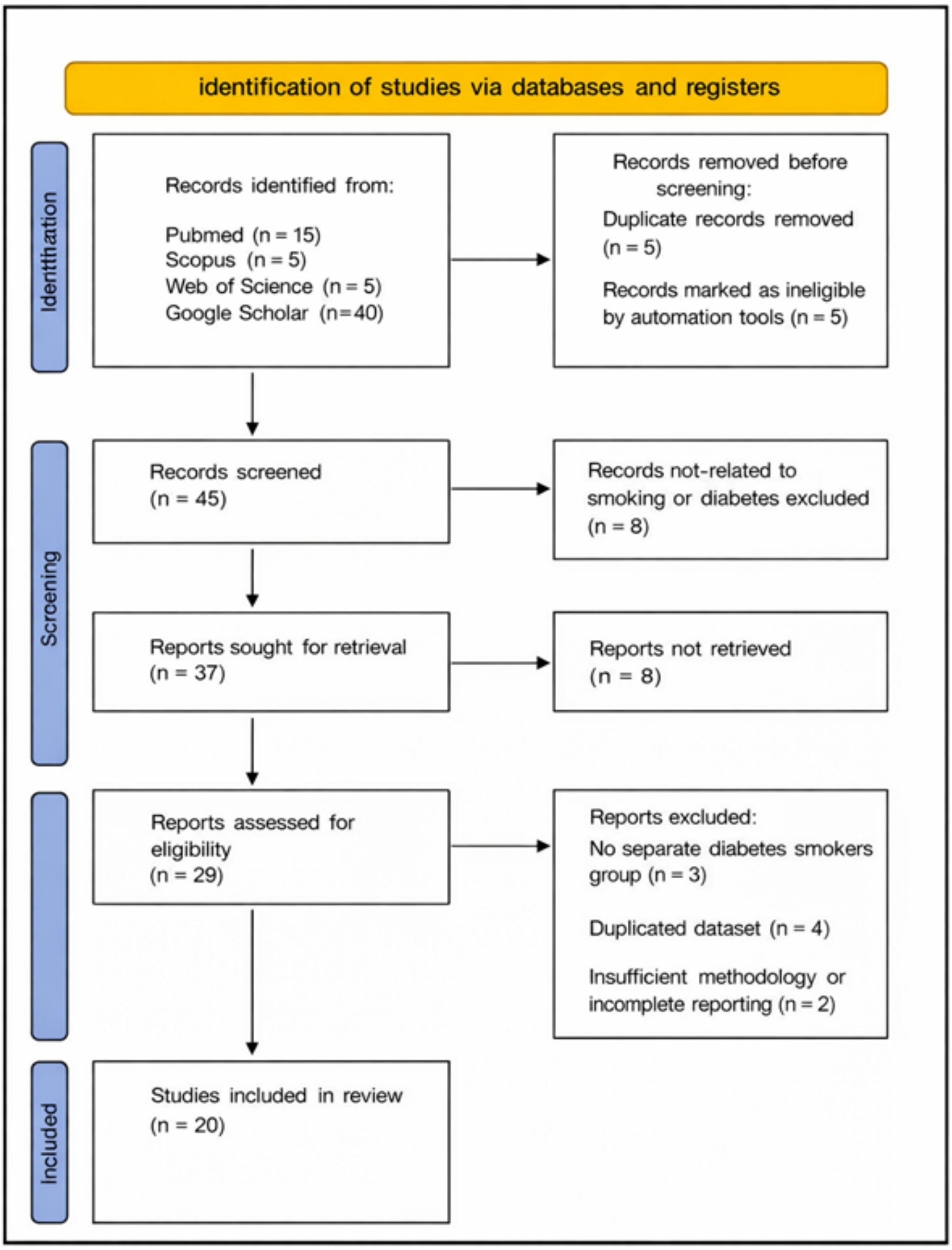

Fig. 1: PRISMA flow chart

As this study was based on previously published data, institutional ethical approval was not required. However, ethical approval details from the included primary studies were recorded whenever available. This was done to maintain transparency and ensure the quality and reliability of the review.

Results: A total of 20 studies were included to evaluate the effects of diabetes and cigarette smoking on retinal structure and microvascular parameters using OCT and OCTA. The detailed characteristics and key findings of most relevant studies are summarized in **Table 1**:

Table 1: Summary of most relevant studies evaluating the effects of diabetes and smoking on retinal structure and microvasculature

Author	Year	Study Design	Population	Exposure	Outcome Measures	Key Findings
Viggiano et al. (2)	2024	Observational	DME patients	Diabetes	OCT biomarkers, retinal thickness	Foveal/parafoveal thickness, ELM status strongly correlated with visual acuity **(p < 0.001).**
Gokmen & Ozgur (3)	2023	Cross-sectional	Smokers vs controls	Smoking	OCTA vascular density	Smoking showed variable effects (↑ deep vascular density, ↓ choroidal thickness with exposure) **(p = 0.011).**
Liu et al. (4)	2021	Cross-sectional	Diabetics without DR	Smoking	OCTA (VLD, FAZ, PD)	Smoking associated with reduced vessel length density, indicating early microvascular damage **(p = 0.046)**.
El Rokh et al. (6)	2021	Prospective	Smokers vs controls	Smoking	Macular, RNFL, choroidal thickness	Smoking significantly reduced macular, RNFL, and choroidal thickness **(p=0.014)**.
Dogan et al. (7)	2020	Cross-sectional	Healthy smokers vs controls	Smoking	OCTA vascular density	Smoking caused reduced deep retinal vascular density **(p=0.01)**.
Gungel et al. (11)	2020	Observational	Diabetic patients	Diabetes	Central macular thickness	CMT influenced by metabolic factors (lipids, glucose, duration) **(p < 0.03)**.
Teberik (12)	2019	Cross-sectional	Healthy smokers vs controls	Smoking	Macular, RNFL thickness	Smoking caused changes in RNFL thickness (sectoral differences) **(p=0.005)**.
Eriş et al. (13)	2019	Observational	Smokers vs non-smokers	Smoking	OCTA perfusion, choroidal thickness	Smoking increased choroidal thickness, no significant perfusion change **(p=0.022)**.
Dong et al. (14)	2017	Case-control	T2DM without DME	Diabetes	Macular thickness (OCT)	Higher homocysteine linked to increased macular thickness **(p = 0.012)**.
Moschos et al. (15)	2016	Case-control	Chronic smokers vs controls	Smoking	Retinal & choroidal thickness	Smoking caused reduced choroidal and retinal thickness.
Dervişoğulları et al. (16)	2014	Observational	Smokers vs controls	Smoking	Retinal & choroidal thickness	No significant change in macular thickness **(p = 0.541)**.

Sng et al. (17)	2012	Cross-sectional	Diabetics with/without DR vs controls	Diabetes	Macular thickness (OCT)	Moderate/severe DR showed increased foveal thickness compared to non-diabetics; no change in early DR **(p = 0.003)**.

DISCUSSION

The study by Viggiano et al. (2024) highlights the importance of OCT-derived biomarkers in patients with diabetic macular edema (DME). Their findings demonstrate that structural parameters such as foveal and parafoveal thickness, along with qualitative markers like ELM integrity, are strongly associated with visual outcomes. This reinforces the concept that retinal morphology plays a critical role in functional recovery. The study supports the use of OCT as not just a diagnostic tool but also a prognostic indicator in diabetic retinal disease. It also emphasizes that even after resolution of edema, subtle structural changes continue to influence vision (2).

Gokmen and Ozgur (2023) explored the impact of chronic smoking on retinal vascular density using OCTA. Their findings suggest a complex relationship, where smoking may increase deep retinal vascular density while simultaneously showing a negative correlation with choroidal thickness over time. This dual effect indicates that smoking may induce both compensatory and degenerative vascular responses. Such variability highlights the need for cautious interpretation of OCTA findings in smokers. The study contributes to understanding how long-term exposure influences retinal microvasculature differently across layers (3).

Liu et al. (2021) provided important insights into early microvascular changes in diabetic patients without visible retinopathy. The study demonstrated that smoking is associated with reduced vessel length density, even before clinical signs of diabetic retinopathy appear. This suggests that smoking may accelerate subclinical retinal damage in diabetic individuals. Their results emphasize the role of OCTA in detecting early vascular compromise. It also underlines the importance of smoking cessation in preventing progression of diabetic retinal disease (4).

El Rokh et al. (2021) investigated the structural impact of smoking on retinal and choroidal layers using SD-OCT. The study found a significant reduction in macular, RNFL, and choroidal thickness in smokers compared to non-smokers. These findings suggest that smoking leads to generalized thinning of ocular tissues, likely due to chronic vascular insufficiency. The negative correlation with smoking exposure further strengthens the dose-dependent effect. This study provides strong evidence for the detrimental structural impact of smoking on the retina (6).

Dogan et al. (2020) focused on retinal vascular density changes in smokers using OCTA. Their results revealed a significant reduction in deep capillary plexus vessel density among smokers. This finding supports the hypothesis that smoking adversely affects retinal microcirculation. The study is particularly important as it shows that even relatively low smoking exposure can lead to measurable vascular changes. It further highlights OCTA as a sensitive tool for detecting early microvascular alterations (7).

Gungel et al. (2020) examined the relationship between central macular thickness and systemic metabolic factors in diabetic patients. Their findings indicate that lipid profile, glucose levels, and disease duration significantly influence macular thickness. This suggests that retinal structural changes in diabetes are multifactorial and closely linked to systemic health. The study reinforces the importance of metabolic control in preventing retinal complications. It also adds depth to the understanding of non-ocular factors affecting retinal morphology (11).

Teberik (2019) evaluated the effect of smoking on macular, choroidal, and RNFL thickness. The study reported sectoral variations in RNFL thickness, indicating that smoking may not affect all retinal regions uniformly. This selective vulnerability could be due to regional differences in vascular supply. The findings highlight the complexity of smoking-induced retinal changes. It also suggests that detailed layer-wise analysis is essential for accurate assessment (12).

Eriş et al. (2019) investigated choroidal thickness and perfusion parameters in smokers using OCTA. The study found increased choroidal thickness in smokers, although perfusion changes were not statistically significant. This paradoxical finding may reflect compensatory vascular responses to chronic hypoxia. It indicates that structural and functional changes may not always align. The study contributes to the ongoing debate regarding the exact impact of smoking on choroidal circulation (13).

Moschos et al. (2016) studied long-term smokers and reported significant thinning of both retinal and choroidal layers. Their findings support the hypothesis that chronic smoking leads to progressive structural degeneration. The long duration of smoking exposure strengthens the evidence for cumulative damage. This study is particularly relevant in understanding the long-term anatomical consequences of smoking. It emphasizes the importance of early lifestyle modification (15).

Sng et al. (2012) provided insights into the effect of diabetes and diabetic retinopathy on macular thickness. Their results showed that significant thickening occurs primarily in moderate to severe stages of retinopathy. This suggests that early diabetes may not always present with detectable structural changes. The study highlights the progressive nature of retinal involvement in diabetes. It also underscores the importance of early screening and monitoring using OCT (17).

Smoking appears to negatively influence both visual function and retinal structure in patients with retinitis pigmentosa. Even after adjusting for age and sex, higher pack-year exposure was independently associated with worse visual acuity, suggesting a direct impact of smoking on disease progression. Structurally, smokers showed reduced ellipsoid zone width and thinner central retinal thickness, indicating greater photoreceptor damage. Although some results were not statistically significant, a consistent trend toward more severe degeneration was observed. These effects may be explained by oxidative stress, vascular compromise, and chronic inflammation induced by smoking, highlighting its role as a modifiable risk factor in RP (18).

Diabetes mellitus (DM) is known to cause widespread vascular alterations, including changes in the diameter of retinal blood vessels, although branching patterns may remain unaffected. Evidence suggests that narrower arteriolar and wider venular calibers are associated with increasing severity of diabetic retinopathy and systemic complications such as nephropathy. Additionally, smoking has been linked to further vascular changes, particularly enlargement of venular caliber, which may worsen retinal microvascular health. However, some OCT-based studies in healthy chronic smokers report no significant differences in retinal layer thickness compared to non-smokers. This indicates that while functional and vascular alterations are evident, structural changes may not always be detectable in early or otherwise healthy individuals (19).

The findings indicate that macular thickness (MT) is significantly lower in females compared to males, consistent with previous studies, although the exact cause of this difference remains unclear. A positive association between body height and MT may reflect variations in ocular anatomy. The relationship between refractive error and MT appears inconsistent, with some studies reporting reduced thickness in high myopia, while others show a positive association. Additionally, decreased MT was associated with hypertension and smoking, suggesting a possible role of vascular and inflammatory mechanisms. Changes in ocular circulation and retinal stress may contribute to this thinning, highlighting the need for further longitudinal studies (20).

Chronic smoking did not produce significant changes in retinal or choroidal thickness. No statistically significant differences were observed between smokers and controls in retinal thickness or choroidal thickness. Additionally, no meaningful correlations were found between ocular or demographic parameters and thickness measurements. Despite evidence of smoking-related vascular dysfunction, structural parameters appeared preserved in this population. These findings suggest that early or moderate smoking exposure may not be sufficient to induce detectable structural retinal changes, although subclinical vascular alterations may still be present (21).

Conclusion: This systematic review highlights that both diabetes mellitus and cigarette smoking have significant effects on retinal structure and microvasculature, as assessed by OCT and OCTA. Diabetes is primarily associated with increased macular thickness and progressive structural changes, particularly in advanced stages of diabetic retinopathy, reflecting the impact of chronic metabolic dysfunction on retinal integrity. Whereas, smoking is predominantly linked to microvascular impairment, including reduced blood vessel density and thinning of retinal and choroidal layers, while some variability exists across studies.

Evidence suggests that smoking may worse subclinical retinal damage in diabetic individuals, even before the onset of clinically visible retinopathy. The use of advanced imaging modalities enables early detection of these changes, offering valuable opportunities for timely intervention. However, variability in the study designs and outcomes indicates the need for further longitudinal and large-scale studies. Overall, these findings highlight the importance of strict metabolic control and smoking cessation as key strategies in preserving retinal health and preventing vision-threatening complications in diabetic populations.

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