A Narrative Review on Dry Eye Disease and Its Determinants in Patients with Diabetes Mellitus

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Abstract: DED is a common ocular condition, particularly in patients with DM. This narrative review discusses the prevalence and determinants of DED among diabetic patients, focusing on glycemic control, duration of diabetes, and diabetic complications, including neuropathy and retinopathy. The paper also presents pathophysiological mechanisms linking DM and DED and proposes recommendations for clinical management and future research. These findings bring importance of early detection and comprehensive management strategies for improving quality of life in patients with diabetes and DED.

Key words: Dry Eye Disease, Diabetes, HbA1c

Introduction

Dry Eye Disease is a complex disorder that disrupts the balance of the tear film, leading to discomfort, visual disturbances, and possible damage to the ocular surface. [1]. It presents mostly with higher osmolarity of the tear film, as well as inflammation of the ocular surface [2]. DED is common in patients with chronic systemic conditions like Diabetes Mellitus, in whom the prevalence is significantly higher when compared with the general population. [3]The prevalence of DED among diabetic patients is remarkably higher than in the general population, and it is, therefore, one of the major concerns in the management of DM. [4][5] This review aims to discuss prevalence, determinants, and implications on the existence of DED in DM patients.

Diabetes can lead to alterations in the tear film and lacrimal glands through multiple pathways. Chronic hyperglycemia can cause biochemical and structural changes in the body, leading to oxidative stress and inflammation that adversely affect tear production and ocular surface health. Diabetic neuropathy, a common complication of DM, impairs corneal sensitivity, which is critical for maintaining normal tear reflexes and responding to ocular surface damage. Additionally, diabetic retinopathy and other vascular changes associated with diabetes can further compromise the health of the ocular surface and contribute to DED.

Prevalence for DED is significantly higher in those with diabetes than those without, an effect of diabetes on ocular surface production and stability. Dry eye symptoms have been reported in studies to occur more in people who have diabetes, and further exacerbation of the symptoms goes hand-in-hand with the duration of diabetes and the glycemic control level.

Understanding the relationship of DM with DED is critical to the improvement of patient outcomes. Effective management of DED in diabetic patients would, therefore, must be holistically approached—one that not only systemically addresses diabetes but also includes the local manifestations of DED. It involves not just the optimization of glycemic control, but institutes targeted measures toward the alleviation of symptoms of dry eye and protection of the ocular surface.

This review provides an overview of the prevalence, determinants, and pathophysiology of DED in diabetes patients. In this context, this review researches the existing evidence of how diabetes influences dry eye conditions and accordingly puts forward some recommendations for clinical practices and future studies.

Factors that enhance the risk of developing DED in Diabetes Mellitus [6,7]:

Duration of Diabetes: The longer the duration of diabetes, the greater the likelihood of DED. In case a patient is having long-term hyper-glycemia for several years, there is an additive effect to accumulated damage of ocular surface and tear production glands.

Poor glycemic control, reflected by high HbA1c levels, had a strong relationship with the incidence and severity of the DED. Inflammation and neuropathic complications of poorly controlled diabetes more likely result in DED.

Diabetic Retinopathy: Patients with diabetic retinopathy, one of the very common microvascular complications of diabetes, are at an increased risk of developing DED. The microvascular changes in the retina may parallel those in the lacrimal glands and ocular surface and thus result in DED.

Insulin use: Some studies have suggested that insulin-treated patients could have an increased risk for DED. This may relate to the duration and severity of the diabetes in these patients, as most insulin-dependent patients had already advanced diseases.

Age and gender: Older age and the female gender are well-established risk factors for the development of DED in the general population and remain significant in patients with T2DM. Postmenopausal women may be at increased risk due to hormonal changes that influence tear production and stability.

Artificial Tears and Lubricants: Over-the-counter artificial tears and lubricants provide some symptomatic improvement in DED by supplementing additional moisture to the ocular surface. Preservative-free formulations must be advised for the patients to avoid further irritation of the ocular surface.

Anti-inflammatory Treatments: Topical anti-inflammatory medications, such as corticosteroids or cyclosporine, are useful in reducing inflammation of the ocular surface and enhancing tear production.

Management of Meibomian Gland Dysfunction: Warm compresses, eyelid hygiene, and certain medications manage MGD, thus enhancing the lipid layer of the tear film and reducing evaporation of the tears.

Management of Neuropathy: Management of diabetic neuropathy using the appropriate medications and making the necessary changes in lifestyle might improve corneal sensitivity and decrease the rate of development of severe DED symptoms.

Methodology

This narrative review includes data from peer-reviewed articles, clinical studies, and expert opinions focusing on DED in diabetic patients. Key databases searched include PubMed, Scopus, and Google Scholar. Keywords used were "dry eye disease," "Diabetes Mellitus," "DED prevalence," "DED determinants," and "diabetic dry eye". From 1990-2024, it included both foundational and recent studies. Reference lists of articles selected were also searched to capture, as broadly as possible, relevant studies that may not have been identified in the initial search. Data were extracted based on study design, sample size, assessment methods, and key results. The review integrates both quantitative data (e.g., prevalence rates, clinical measures) and qualitative data (e.g., patient-reported outcomes, expert opinions). Key determinants of DED and their associations with diabetes management and complications were identified.

Inclusion and Exclusion Criteria

Inclusion criteria:

- Studies assessing the prevalence or severity of DED in diabetic patients.
- Research on diabetes management's impact on DED.
- Clinical trials or observational studies with relevant outcomes.

Exclusion criteria:

- Non-diabetic dry eye studies.
- Research focused solely on non-diabetic dry eye.
- Research without full-text availability or adequate methodological details.

Data synthesis involved grouping findings into themes related to prevalence, severity, and determinants of DED in diabetic patients. Comparative analyses were conducted to highlight consistent findings and discrepancies. The review also considered the impact of diabetes management on DED outcomes.

Results

Most of the studies have invariably reported a higher frequency of DED in diabetic patients compared with nondiabetic individuals. For example, a comprehensive study from Japan reported that 54% of type 2 diabetic patients had symptoms of DED, which is significantly higher than the 30% prevalence noted in nondiabetic controls [8]. In another study from India, it was found that the prevalence of DED was 28% among type 2 diabetic patients, as against 12% in nondiabetic subjects. [9]. In the USA, about 20% of people living with diabetes suffer from symptoms of DE, underscoring again how important this condition is in diabetic populations.[10].

Determinants of DED in Diabetic Patients:

- Metabolic Control: Glycemic control is a major determinant for initiation and progression of DED. Some studies have demonstrated that higher HbA1c, as a marker of long-term glycemic control, is strongly related to increased severity of symptoms of DED [11, 12]. Poorly managed diabetes will, by default, involve ocular surface damage to a greater degree and is thus a contributory factor to the increased prevalence of DED in this population.
- Duration of Disease (DM): This has been observed to be a major determinant of risk for DED. Indeed, using the data available from Italy, it has been reported that patients with more than 10 years of diabetes had a 2.5-fold increased risk for DED when compared to those with a shorter duration of diabetes [13]. This relationship underscores the cumulative effect of chronic hyperglycemia and its impact on tear film stability over time.

- Neuropathy and retinopathy in diabetes: Diabetic complications, especially neuropathy and retinopathy, have a strong link with DED. A study from Turkey revealed that patients with proliferative diabetic retinopathy had a higher prevalence of DED, thus indicating that changes at the retina level could exacerbate the symptoms of dry eye. [14]. Moreover, diabetic neuropathy, which is associated with decreased corneal sensation, also leads to a decrease in tear production and aggravation of dry eye symptoms. [15].
- Inflammation: In patients with diabetes and DED, systemic inflammatory markers, such as elevations in C-reactive protein and interleukin-6, are correlated with more severe dry eye symptoms, pointing to the fact that inflammation has a central role in the pathogenesis of DED in diabetes [16, 17].

Discussion

The high prevalence of DED in this group of diabetic patients warrants enhanced awareness by both the patient and the healthcare professional regarding disease management. A multiple and very complex pathophysiological link between DM and DED leads to chronic hyperglycemia, subsequently inducing oxidative stress and advanced glycation end products (AGEs), which cause inflammation and damage to the lacrimal glands and ocular surface tissues. [18, 19]. This contributes to decreased tear production and tear film instability, which are characteristic of DED.

Diabetic neuropathy, particularly corneal neuropathy, is important in the development of DED. Diminished corneal sensitivity in diabetic patients impairs reflex tear secretion, leading to a reduced capacity of protection and ocular surface lubrication. Besides, diabetic retinopathy is associated with changes in the microvasculature that may aggravate ocular surface deterioration and further raise the risk of developing DED [20,21].

The high prevalence of DED in patients with diabetes thus justifies routine screening for the disease and institution of early intervention. Such comprehensive management strategies ought to be oriented toward the optimization of glycemic control, since better management of blood sugar levels is related to a reduction in the severity of DED [22, 23]. Exogenous artificial tears and ocular lubricants, when used regularly, can be helpful in stabilizing the tear film and alleviating symptoms [24]. In cases of patients with high inflammation, topical anti-inflammatory therapy could be useful, with corticosteroids or cyclosporine [25].

In patients with diabetes, the management of DED must be multi-faceted, directed both at systemic and ocular features. In addition to blood glucose management, other causative underlying cofactors for dry eye should be controlled. Symptomatic management directed at inflammation includes the use of anti-inflammatory agents for the treatment of more serious cases of DED [26].

Future works should be centered on the actual ways through which DM exacerbated DED. Further investigation of the roles of inflammation, oxidative stress, and neuropathy in the mechanism of DED must be done towards more targeted therapeutic interventions. Clinical trials to evaluate the new drugs' efficacy in the treatment of DED among diabetic patients are also of utmost importance for ameliorating the patients' outcome management strategies [27, 28].

Limitations

Cross-Sectional Nature: Many studies included are cross-sectional, limiting the ability to establish causation. Longitudinal studies are needed to assess the progression of DED and its determinants.

Sample Diversity: Limited sample sizes and diversity in studies may affect the generalizability of findings. Larger, more diverse samples are needed for broader applicability.

Variability in Measurement Methods: Differences in assessment techniques for DED across studies can affect comparability. Standardizing assessment methods would improve consistency.

Potential Confounders: Factors such as environmental conditions, lifestyle habits, and comorbidities were not always accounted. Future research should consider these potential confounders e.g., other medications or comorbid factors that may impact tear production and ocular surface health.

Chance for bias in a subjective assessment of symptoms (dry eye), which were self-reported, and questionnaire assessments which may result in systematic under- or overreporting. In addition, the study population was quite different relying on patients attending a diabetes clinic and selection bias may occur which makes our result less generalizable to all T2DM patients.

Strengths

Comprehensive Review: This review provides a thorough examination of DED prevalence, determinants, and management in diabetic patients, synthesizing data from a range of studies.

Integration of Data: The review combines objective clinical measures with patient-reported outcomes, offering a holistic view of DED impact

Focus on Diabetes Management: Emphasis on diabetes management's impact on DED severity highlights practical implications for clinical practice

DED and its Determinants were Discussed: This helps in establishing valuable insights for future research and specific interventions.

The current study has several limitations and strengths. Among the former, the sample size is large, improving statistical sensitivity and result consistency. This therefore increases the evidence base for associating T2DM with DED. By addressing dry eye in a well-characterized population of T2DM patients, the study could contribute to our understanding of how management may differ in that setting.

Conclusion

DED is a common and clinically significant complication of DM. Based on the high prevalence and multifactorial pathogenesis of DED in diabetic patients, there is a need for comprehensive management strategies targeting systemic and ocular factors [29]. Attention to optimal glycemic control and the use of targeted ocular therapies could improve outcomes in patients with diabetes andDED [30,31].

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Conflict of Interest

None

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