

# World Journal of *Diabetes*

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Peer Review of *World Journal of Diabetes*, Erkan Gokce, MD, Professor, Department of Radiology, Tokat Gaziosmanpasa University, School of Medicine, Tokat 60100, Türkiye. drerkangokce@gmail.com

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*WJD* mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

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## Bidirectional link between periodontitis and systemic inflammation in diabetic retinopathy

Prateek Nishant, Sony Sinha, Ranjeet Kumar Sinha, Arvind Kumar Morya

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**Prateek Nishant**, Department of Ophthalmology, ESIC Medical College, Patna 801103, Bihar, India

**Sony Sinha**, Department of Ophthalmology-Vitreo-Retina, Neuro-Ophthalmology and Oculoplasty, All India Institute of Medical Sciences, Patna 801507, Bihar, India

**Ranjeet Kumar Sinha**, Department of Community Medicine, Patna Medical College, Patna 800004, Bihar, India

**Arvind Kumar Morya**, Department of Ophthalmology, All India Institute of Medical Sciences, Hyderabad 508126, Telangana, India

**Corresponding author:** Arvind Kumar Morya, Additional Professor, Head of the Department, Department of Ophthalmology, All India Institute of Medical Sciences, Bibi Nagar, Hyderabad 508126, Telangana, India. [bulbul.morya@gmail.com](mailto:bulbul.morya@gmail.com)

### Abstract

Periodontitis is independently associated with numerous lifestyle diseases. Diabetic patients have approximately threefold increased odds of periodontitis, which in turn increases the risk of systemic inflammation. The study by Thazhe Poyil *et al* is an effort to establish the inflammatory link between diabetic retinopathy (DR) and periodontitis based on the periodontal inflamed surface area in diabetic patients with and without DR. To further advance the study, we suggest refining the eligibility criteria to explicitly state the clinical correlates of periodontitis and DR, larger sample size and improved sampling methodology, matching of baseline characteristics of the two groups, as well as improved statistical approach and interpretation of the study findings. Measurement of hemoglobin A1c (HbA1c) in studies comparing type 2 diabetes mellitus patients with DR of matched severity with and without periodontitis could provide a clearer picture of whether HbA1c level is indeed influenced by periodontitis.

**Key Words:** Glucose intolerance; Hyperglycemia; Inflammation; Research methodology; Vision

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**Core Tip:** The study by Thazhe Poyil *et al* is an effort to establish the inflammatory link between diabetic retinopathy (DR) and periodontitis based on the periodontal inflamed surface area in diabetic patients with and without DR. To further advance the study, we suggest refining the eligibility criteria to explicitly state the clinical correlates of periodontitis and DR, larger sample size and improved sampling methodology, matching of baseline characteristics of the two groups, as well as an improved statistical approach and interpretation of the study findings.

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## TO THE EDITOR

We read with great interest the study by Thazhe Poyil *et al*[1], and congratulate the authors on their effort to establish the inflammatory link between diabetic retinopathy (DR) and periodontitis based on the periodontal inflamed surface area in diabetic patients with and without DR[1,2].

The authors have chosen a contemporary topic affecting the health of diabetic patients, and have examined their concerns for periodontal complications in these patients in type 2 diabetes mellitus (T2DM) subjects by comparing groups of 40 patients with DR and 40 without DR; comparison was also made with non-proliferative DR and proliferative DR subgroups. This is relevant because periodontitis is independently associated with numerous lifestyle diseases which primary care physicians and oral health professionals should be aware of[3].

The authors have analyzed various clinical and biochemical parameters. Most of the results have shown a positive correlation between poorer glycemic control, inflammatory markers and clinically observed periodontal inflammation scores, as could be expected from the current understanding of diabetes mellitus as a systemic inflammatory condition[4].

It is known that diabetic patients have approximately threefold increased odds of periodontitis. Chronic periodontitis increases the risk of systemic inflammation which may adversely affect glycemic control in diabetic patients[5]. This has correctly been called a “bidirectional link”[6]. We wish to add to the authors’ conclusions by stressing the following, which when considered could have further reinforced the evidence obtained by the study.

It is known that co-existing ocular pathologies can alter the diagnosis and progression of DR. Also, several monocular conditions lead to a picture of asymmetric DR, which could have led to fallacies in categorizing the patients as having non-proliferative or proliferative DR[7]. It is unclear if the patients in the groups had similar ocular characteristics as the occurrence of such conditions has not been stated as an exclusion criterion. It is also not clear whether any cases with asymmetric DR were found or excluded. We suggest refining the eligibility criteria of the study to explicitly state the clinical correlates of periodontitis and DR.

In the study, periodontitis occurred in 47.5% and 27.5% of patients of T2DM with and without DR respectively[1]. However, at baseline, there was a significant difference in gender distribution between the two groups, with the DR group having more male subjects. A growing body of research suggests that sex has an impact on a variety of systemic illnesses including diabetes, with differences being observed in systemic inflammatory parameters due to differences in hormones, body composition, physiological differences in glucose and fat metabolism, and even gut microbiota[8]. Similarly, the groups had statistical differences in the duration of diabetes and hemoglobin A1c (HbA1c) detected at baseline, indicating distinct differences in the consistency of glycemic control. In addition, there is no mention of the range and skewness of plasma glucose levels (fasting and post-prandial) in the groups, nor any statistical test to determine the normality of data has been reported. A true comparison of periodontal variables is only possible if the patients are comparable as regards the other ocular characteristics. The confounding effect of gender and status of glycemic control should be considered while comparing the probability of periodontitis in DR, and the effect corrected using regression analysis or other statistical methods if dissimilar at baseline[9]. Improved sampling methodology and matching of baseline characteristics of the two groups may also help in overcoming such limitations.

The study reported mild periodontitis to be present in 75.0% of patients of T2DM without DR. This proportion was 52.5% in patients of T2DM with DR. However, this is not reflected in the figure provided in that study, which shows the said proportion among patients with T2DM without DR to be 7.5%[1]. Given that levels of all the periodontal variables are higher in the group of T2DM with DR, it appears to be erroneously mentioned that 75.0% (three-fourths) of all patients have mild periodontal inflammation in the presence of better periodontal parameters in the group of T2DM without DR.

The authors have stated that HbA1c level in T2DM patients with and without DR could have been affected by periodontal inflammation. We believe that measurement of HbA1c in studies comparing T2DM patients with DR of matched severity with and without periodontitis could provide a clearer picture of whether HbA1c level is indeed influenced by periodontitis, and if so, whether the severity of periodontitis is correlated well with HbA1c levels in the absence of other modifying factors as previously observed in patients without diabetes as well[10,11].

Finally, the study has compared 40 patients in each group without sample size justification and power calculation. Given that previous studies with similar sample size have shown similar results, further studies with larger sample sizes are required, because low sample sizes in current and previous studies have led to poor precision analysis of the

association between periodontitis and DR[12].

## FOOTNOTES

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**Country of origin:** India

**ORCID number:** Prateek Nishant 0000-0003-3438-0040; Sony Sinha 0000-0002-6133-5977; Arvind Kumar Morya 0000-0003-0462-119X.

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