ASSOCIATION OF SERUM VITAMIN D LEVELS WITH PERIODONTITIS IN TYPE 2 DIABETIC SUBJECTS IN A TERTIARY CARE UNIT OF KARACHI

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Author's Contribution:

M.M. created the model and computational framework, as well as analyzed the data. A.F. supervised the study. E.A. carried out the calculation. The manuscript was written by M.M. with input from all authors. S.A. managed the drafting of manuscript. I.A and A.B. provided overall guidance and direction of the project.

ABSTRACT

Objective: The current study aimed to examine the relationship of vitamin D levels with periodontitis in subjects with type 2 diabetes and to determine whether there is an association of glycemic control with periodontitis.

Methods: The present observational study conducted with a total of 112 participants allocated equally into two groups. Group 1, 56 diabetic without periodontitis were taken as Control and Group 2, 56 diabetic with periodontitis as Cases. Subjects with Type 1 and Gestational Diabetes were not included. Subjects on Vitamin D supplements, pregnant and lactating females were excluded. The research was carried out at Dental Clinics of Baqai Institute of Diabetology and Endocrinology, Baqai Medical University, Karachi. Anthropometric and biochemical parameters were measured. Anthropometric parameters incorporated height, weight, and BMI while biochemical comprised of vitamin D and HbA1c. Periodontitis was evaluated using CPITN index. Data was analyzed by using SPSS version 23. Continuous variables were presented as Mean± standard deviation while categorical variables were presented as Frequency (percentage). Analysis of variables was done by Student's T-test, ANOVA, and Chi-square test, as appropriate p value<0.05 considered to be statistically significant.

Results: Poor glycemic control i.e. (HbA1c>8) was prevalent in 87.5 % of diabetic subjects with periodontitis while it was present in 66.1 % without periodontitis with statistically significant difference (p=0.007). HbA1c levels were inversely and significantly associated with periodontal disease (p=0.013). In periodontitis group low vitamin D levels were significantly prevalent as compared to the non-periodontitis group (p 0.001).

Conclusion: Individuals with periodontitis and type 2 diabetes may have reduced vitamin D levels which seems to be linked with inflammation and also has an impact on glycemic status.

Key words:

Diabetes, Periodontitis, Serum Vitamin D, Glycemic control

INTRODUCTION

Periodontitis is a chronic inflammatory disease of the oral cavity that affects 10% to 15% of the population, resulting in chronic pain with incidence of loss of teeth and supporting tissues [1]. It develops when untreated gingivitis causes the loss of gingiva, bone, and ligament, resulting in the formation of periodontal pockets, a defining feature of the disease that eventually leads to tooth loss [2]. Periodontitis is no longer perceived as a local phenomenon. Instead, it is an inflammatory disease that can lead to numerous systemic changes. [3] Factors like diabetes or vitamin D deficiency are known to intensify inflammatory responses, which leads to more periodontal destruction. [4]

Inflammation marks the link between diabetes and periodontal disease. [5] Diabetes affects the periodontal tissues by creating changes in host defense, collagen metabolism, as well as vascular changes, leads to a more inflammatory response to pathogens of periodontitis. [6] The increase in the risk of severity of periodontitis is recognized to be reliant on glycemic control, and so is the risk of all diabetes complications. Consequently, in well-controlled diabetes with HbA1c levels of around 7% (53 mmol/mol) or lower, diabetes appears to have little effect on periodontitis risk. The risk, however, grows exponentially as glycemic control deteriorates. Overall, diabetes is thought to raise the risk of periodontitis by 2-3 folds – that is, it raises the risk of periodontitis by 23 times [7].

Vitamin D and its active metabolite 1, 25 dihydroxy vitamin D (25(OH) D) has anti-inflammatory characteristic. It has recently been proposed that its anti-inflammatory activity is responsible for its effects on ailment of periodontal environment, dentate shortfall, and contamination at the gingivae. [8] A number of reports have suggested that there is a close connection between the periodontal health and 25 (OH) D statuses [9, 10]. Declined 25(OH) D could be the outcome of inflammatory processes involved in the occurrence and disease process [11]. Vitamin D plays an important role in regulating insulin activity and direct stimulation of the genes of the insulin receptor. Several cross-sectional studies have shown a reverse relationship between serum 25(OH)D concentrations and insulin resistance [12,13]. Therefore, the current study was done to scrutinize the relationship of vitamin D levels with periodontitis with demographic using a representative sample of Type 2 subjects.

MATERIAL AND METHODS

The current research was an observational case-control study. The research was carried out at Dental Clinics of Baqai Institute of Diabetology and Endocrinology, Baqai Medical University Karachi. The study was conducted between June 2021 to November 2021 after approval from Ethics Review Committee and BASR. A total of 112 subjects (males and females) were included in the study. An informed consent was taken from every participant prior to the study. The study participants were divided into two groups: (i) Controls, 56 diabetic without periodontitis were

taken as Control (ii) Cases, 56 diabetic with periodontitis as Cases. Subjects with Type 1 Diabetes Mellitus and Gestational Diabetes were not included. Subjects on Vitamin D supplements and Pregnant and lactating females were excluded. Subjects having any malignancy, malabsorption syndrome or chronic diarrhoea were excluded. Subjects with history of chronic diseases and autoimmune diseases were excluded.

The data was collected using a two-part questionnaire as a research instrument. The first section of the questionnaire included demographic information about patients, including the age, gender, marital status, occupation, and BMI. The biochemical including HbA1C and Vitamin D levels were measured and noted in the second section of the questionnaire. This section also includes the Community Periodontal Index of Treatment Needs (CPITN), which is used to investigate bleeding on probing and clinical attachment loss.

For the examination of periodontitis William's graduated periodontal probe was used for all teeth on six locales, a test was utilized to survey pocket profundity (PD), gingival downturn, and clinical connection misfortune (CAL) (mesio-buccal, mid-buccal, disto-buccal, mesiolingual, mid-lingual, and disto-lingual). The clinical assessment was directed by a solitary prepared inspector. The severity of periodontitis can be described as mild, moderate, or severe. Mild periodontitis is defined as having CAL of 1–2 mm, moderate periodontitis describes CAL of 3–4 mm, and severe form is defined as CAL of 5 mm or more [14].

The cc blood was obtained and kept in EDTA to prevent coagulation. The serum was separated for the estimation of Vitamin D. HbA1c was measured by High Performance Liquid Chromatography (HPLC) [15] using Bio Rad D-10 automatic analyzer. The level of Vitamin D was measured using an electro-chemiluminescence immunoassay [16]. Vitamin D levels were classified 30 ng/ml as normal, insufficient as 20–30 ng/ml and deficient as <20 ng/ml. [17]

RESULTS

The comparison of basic characteristics between subjects with periodontal disease and without periodontal disease is shown in **Table 1**. Gender ratio was found equal in both groups (p<0.05). Type 2 diabetic subjects with periodontal disease were significantly older with the mean age of 52.66±1.3 years and had longer duration of diabetes as 27(48.2%) had diabetes for more than 5 years than subjects without periodontal disease (p < 0.05). The weight and height were found significantly lower in those who had periodontitis (p<0.05). No significant difference was found in smoking habit and treatment modality of both groups (p>0.05).

Parameters	Subjects with	Subjects without	p-value
	periodontal disease	periodontal disease	
	(n=56)	(n=56)	
Gender			
Male	28(50%)	30(53.6%)	0.705
Female	28(50%)	26(46.4%)	
Age (years)	52.66±1.3	44.21±1.3	< 0.001
Weight (kg)	74±2.1	81.68±2.38	0.017
Height (cm)	161.2±1.25	165.82±1.17	0.008
Body mass index	28.56±0.83	29.66±0.78	
(kg/m^2)			
Smoking habit			
No	52(92.9%)	51(91.1%)	0.728
Yes	4(7.1%)	5(8.9%)	
Treatment Modality			
OHA	40(71.4%)	40(71.4%)	0.565
Insulin	3(5.4%)	1(1.8%)	
Both	13(23.2%)	15(26.8%)	
Diabetes of diabetes	7.73±0.99	4.15 0.65	0.009
(years)			
≤5 years	29(51.8%)	40 (71.4%)	0.033
>5 years	27(48.2%)	16(28.6%)	

 Table 1: Comparison of basic characteristics between subjects with periodontal disease and without periodontal disease

Data presented as mean±standard error or n (%)

 $P\text{-value}{<}0.05 \text{ considered to be statistically significant}$

Chi square Test and independent samples t test applied

Table 2 shows a comparison of biochemical parameters between subjects with and without periodontal disease and it was found that HbA1c was significantly higher in subject with periodontitis as compared to their counterparts without periodontitis (p 0.013), and Vitamin D levels were found to be statistically higher in subjects without periodontitis as compared to the other group with periodontitis (p < 0.001).

Parameters	Subjects with periodontal disease (n=56)	Subjects without periodontal disease (n=56)	t test	p-value
HbA1c	9.86 ± 2.18	8.90 ± 1.82	2.533	0.013
Vitamin D	26.04 ± 8.35	32.19 ± 9.29	-4.415	<0.001

 Table 2: Comparison of bio-chemical parameters between subjects with periodontal disease

 and without periodontal disease

Figure 1 shows the association of HbA1c with periodontitis and it is seen that poor glycemic control (HbA1c >8) was prevalent in 87.5 % subjects with periodontitis, while it was present in 66.1 % subjects without periodontitis and significant difference was observed between the study groups (p = 0.007).



Figure 1: Association of HbA1c levels with Periodontitis

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Figure 2 presented the association between vitamin D and periodontitis and it was observed that vitamin D deficiency (25%) and insufficiency (41.1%) was significantly higher in subjects with periodontitis as compared to subjects without periodontitis in which deficiency of vitamin D was found in 5.3% and insufficiency was 17.9% subjects. Relatively, normal vitamin D levels were significantly lower in subjects with periodontitis (33.9%) as compared to group without periodontitis (76.8%) (p < 0.001).



Figure 2: Association of Vitamin D levels with Periodontitis

DISCUSSION

The present study reports a strong significant association between vitamin D levels and periodontitis and it was observed that vitamin D deficiency and insufficient was more prevalent in diabetic subjects with periodontitis as compared to the diabetic subjects without periodontitis (p < 0.001). Similar findings were concluded in previous studies that showed a strong association of vitamin D levels with periodontitis in type 2 diabetic subjects [18, 19]. This association is evident

as it was previously defined that vitamin D has critical job in bone digestion, antimicrobials impacts against periodontal microorganisms, and potential to obstruct provocative cytokines that animate periodontium injury [20]. However, a recent study shows contradictory results and reported a non-significant association between vitamin D levels and periodontitis [4]. This may be due to the effect of vitamin D supplementation as most of the study participants in the study were taking supplementation of vitamin D.

The association of glycemic control with periodontitis shows that glycemic control is a significant predictor of periodontitis in subjects with type 2 diabetes as periodontitis was seen significantly higher in diabetic subjects with HbA1c > 8 as compared to their counterparts with lower HbA1c (p = 0.007). Previously, Chandna et al. identified periodontitis as a recognized complication of diabetes, and found that it was more common among people with poor glycemic control [21]. Moreover, Tsai et al. also discovered that poorly controlled diabetes had a significantly higher incidence of chronic periodontitis and its associated complications [22]. The possible explanation of this causal relationship may reside in a fact that periodontitis and type 2 diabetes independently, have elevated inflammatory markers however, when present at the same time, there is an exacerbation of this immunoinflammatory response [23]. The association of periodontitis with type 2 diabetes also verified by the duration of diabetes, higher frequency of patients with periodontitis had longer duration of diabetes (Table 1). This shows the exacerbating effect of diabetes on dental health.

The mean serum level of vitamin D also shows the bidirectional relation between periodontitis and vitamin D in type 2 diabetes. It is seen in the present study that mean serum levels of vitamin D are lower in diabetic subjects with periodontitis (26.04 ± 8.35) as compared to the diabetic subjects without periodontitis (32.19 ± 9.29) with statistically significant difference (p <0.001) Table 2. It is also shown that HbA1c levels were significantly higher in diabetic subjects with periodontics (9.86 ± 2.18) in comparison to the other diabetic group without periodontitis (8.90 ± 1.82) (p, 0.013). This relationship was also witnessed in the previous report that shows low serum vitamin D level in chronic periodontitis patients with type 2 diabetes [24].

The study is not without limitation. Small sample size and cross sectional nature are among the considerable limitations of the study.

CONCLUSION

The study concluded that low vitamin D is concomitant to chronic periodontitis. It not only triggers inflammation in the periodontium but also has an impact on glycemic status. As a result, individual with periodontitis and type 2 diabetes might have low Vitamin D. However, before vitamin D supplementation might be proposed for the avoidance of periodontitis in those containing diabetes or not, randomized preliminaries are expected to affirm these discoveries.

CONFLICT OF INTRERSET: There is no conflict of interest.

REFERENCES

1. Gupta V, Mishra S, Gazala MP, Vandana KL, Ratre MS. Serum Vitamin D level and its association with red blood cell indices in patients with periodontitis. Journal of Indian Society of Periodontology. 2022 Sep 1;26(5):446-50.

2. Klokkevold PR, Newman MG, Takei HH, editors. Carranza's clinical periodontology. Elsevier Saunders; 2015.

3. Carrizales-Sepúlveda EF, Ordaz-Farías A, Vera-Pineda R, Flores-Ramírez R. Periodontal disease, systemic inflammation and the risk of cardiovascular disease. Heart, Lung and Circulation. 2018 Nov 1;27(11):1327-34.

4. Akbari N, Hanafi Bojd M, Goldani Moghadam M, Raeesi V. Comparison of serum levels of vitamin D in periodontitis patients with and without type 2 diabetes and healthy subjects. Clinical and Experimental Dental Research. 2022 Dec;8(6):1341-7.

5. Verhulst MJ, Loos BG, Gerdes VE, Teeuw WJ. Evaluating all potential oral complications of diabetes mellitus. Frontiers in endocrinology. 2019 Feb 18;10:56.

6. Agrawal AA, Kolte AP, Kolte RA, Chari S, Gupta M, Pakhmode R. Evaluation and comparison of serum vitamin D and calcium levels in periodontally healthy, chronic gingivitis and chronic periodontitis in patients with and without diabetes mellitus–a cross-sectional study. Acta odontologica scandinavica. 2019 Nov 17;77(8):592-9.

7. Akram Z, Alqahtani F, Alqahtani M, Al-Kheraif AA, Javed F. Levels of advanced glycation end products in gingival crevicular fluid of chronic periodontitis patients with and without type-2 diabetes mellitus. Journal of periodontology. 2020 Mar;91(3):396-402.

8. Meghil MM, Hutchens L, Raed A, Multani NA, Rajendran M, Zhu H, Looney S, Elashiry M, Arce RM, Peacock ME, Dong Y. The influence of vitamin D supplementation on local and systemic inflammatory markers in periodontitis patients: A pilot study. Oral diseases. 2019 Jul;25(5):1403-13.

9. Perić M, Cavalier E, Toma S, Lasserre JF. Serum vitamin D levels and chronic periodontitis in adult, Caucasian population—a systematic review. Journal of periodontal research. 2018 Oct;53(5):645-56.

10. Jagelavičienė E, Vaitkevičienė I, Šilingaitė D, Šinkūnaitė E, Daugėlaitė G. The relationship between vitamin D and periodontal pathology. Medicina. 2018 Jun 12;54(3):45.

11. Autier P, Boniol M, Pizot C, Mullie P. Vitamin D status and ill health: a systematic review. The lancet Diabetes & endocrinology. 2014 Jan 1;2(1):76-89.

12. Grammatiki M. Abstract: Vitamin D and diabetes mellitus: Vitamin D and diabetes mellitus: Causal or casual association? Reviews in Endocrine and Metabolic Disorders, 18, 1–5.

13. Das G. Vitamin D and type 2 diabetes. Practical Diabetes. 2017 Jan;34(1):19-24b.

14. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. Journal of periodontology. 2018 Jun;89:S159-72.

15. Dildar S, Imran S, Naz F. Method comparison of Particle Enhanced Immunoturbidimetry (PEIT) with High Performance Liquid Chromatography (HPLC) for glycated hemoglobin (HbA1c) analysis. Clinical Diabetes and Endocrinology. 2021 Dec;7:1-5.

16. Babić N. Analytical methods and performance of the immunoassay methods for determination of vitamin D in comparison to mass spectrometry. Journal of Medical Biochemistry. 2012;31(4):333-8.

17. Samrah S, Khatib I, Omari M, Khassawneh B, Momany S, Daoud A, Malkawi M, Khader Y. Vitamin D deficiency and level of asthma control in women from North of Jordan: a case–control study. Journal of Asthma. 2014 Oct 1;51(8):832-8.

18. Machado V, Lobo S, Proença L, Mendes JJ, Botelho J. Vitamin D and periodontitis: A systematic review and meta-analysis. Nutrients. 2020 Jul 22;12(8):2177.

19. Perić M, Cavalier E, Toma S, Lasserre JF. Serum vitamin D levels and chronic periodontitis in adult, Caucasian population—a systematic review. Journal of periodontal research. 2018 Oct;53(5):645-56.

20. Anand N, Chandrasekaran S, Rajput NS. Vitamin D and periodontal health: Current concepts. Journal of Indian Society of Periodontology. 2013;17[3]:302.

21. Chandna S, Bathla M, Madaan V, Kalra S. Diabetes mellitus-a risk factor for periodontal disease. Internet J Family Prac. 2010;9[1]:181-4.

22. Tsai C, Hayes C, Taylor GW. Glycemic control of type 2 diabetes and severe periodontal disease in the US adult population. Community dentistry and oral epidemiology. 2002;30(3):182-92.

23. Portes J, Bullón B, Quiles JL, Battino M, Bullón P. Diabetes mellitus and periodontitis share intracellular disorders as the main meeting point. Cells. 2021 Sep 13;10(9):2411.

24. Joseph R, Nagrale AV, Joseraj MG, Kumar KM, Kaziyarakath JA, Chandini R. Low levels of serum Vitamin D in chronic periodontitis patients with type 2 diabetes mellitus: A hospital-based cross-sectional clinical study. Journal of Indian Society of Periodontology. 2015 Sep;19(5):501.