DOI: 10.4274/gulhane.galenos.2024.42713 Gulhane Med J 2024;66(3):133-138



Relationship between glycemic control and oral health status in patients with type 2 diabetes mellitus

Bharathi Ashok Kumar, Nina Shenoy, Kolluru Subhash Chandra, Ashatha Shetty

Nitte (Deemed to be University), AB Shetty Memorial Institute of Dental Sciences (ABSMIDS), Department of Periodontics, Mangalore, India

Cite this article as: Kumar BA, Shenoy N, Chandra KS, Shetty A. Relationship between glycemic control and oral health status in patients with type 2 diabetes mellitus. Gulhane Med J. 2024;66(3):133-138

Date submitted: 16.01.2024

Date accepted: 30.05.2024

Online publication date: 03.09.2024

Corresponding Author:

Nina Shenoy, MDS, Prof., Nitte (Deemed to be University), AB Shetty Memorial Institute of Dental Sciences (ABSMIDS), Department of Periodontics, Mangalore, India +0091-9844344488 drninavijaykumar@nitte.edu.in

ORCID: orcid.org/0000-0002-1189-6901

Keywords: Diabetes, glycemic control, periodontitis, xerostomia, hyposalivation, oral health

ABSTRACT

Aims: Diabetes mellitus (DM) is associated with dry mouth, reduced saliva, taste changes, and periodontal disease. This study aimed to evaluate and determine the correlation between oral health status and glycaemic control levels in patients with type 2 DM (T2DM).

Methods: This cross-sectional study was conducted on patients with T2DM aged 35-65 years. Glycemic control levels were categorized as good control (≤7% of HbA1c) and poor control (>7% of HbA1c). Full mouth plaque score (FMPS), full mouth bleeding score (FMBS), probing depth (PD), and clinical attachment level (CAL) were determined, along with xerostomia (using a standard questionnaire) and hyposalivation (using modified Schirmer test, MST).

Results: This study included 70 individuals with T2DM, comprising 49 males (70%) and 21 females (30%) with a mean age of 55.36±8.3 and 49.36±6.8 years, respectively. Among those with poor glycemic control, a significantly higher prevalence of xerostomia (52.2%), hyposalivation (47.8%), and periodontitis (moderate; 47.8% and severe; 21.7%) was observed compared with those with good control (p=0.027, 0.001, 0.007, respectively). HbA1c exhibited a significant moderate positive correlation with FMPS (r=0.447; p=0.001) and a low correlation with FMBS (r=0.283; p=0.018) and CAL (r=0.301; p=0.011).

Conclusions: The study concluded that individuals with poor glycemic control for T2DM have a higher incidence of xerostomia, hyposalivation, and compromised periodontal health, resulting in a decline in their oral health status.

Introduction

The development of type 2 diabetes mellitus (T2DM), a common metabolic disorder worldwide, is primarily driven by two key factors: dysfunctional insulin secretion from pancreatic β -cells and the resistance of insulin-sensitive tissues to insulin action (1). Periodontitis is an inflammation-induced disease affecting the supportive tissues of teeth. It is caused by specific microorganisms or groups of closely related microorganisms, leading to the gradual destruction of the periodontal ligament and alveolar bone, accompanied by increased probing depth

(PD), gingival recession, or both (2). Periodontitis is the sixth consequence of diabetes mellitus (DM), and both type 1 DM (T1DM) and T2DM are significant risk factors for periodontal disease (3). Patients with T2DM may be more susceptible to or experience a more severe periodontal disease if they have poor glycemic control. Moreover, periodontitis has a systemic link with adverse cardiovascular outcomes. Furthermore, subsequent tooth loss associated with periodontitis can lead to deleterious dietary modifications, potentially worsening comorbidities in patients with T2DM (4).



Saliva, the main environment for oral flora, mechanically cleanses the remnants of nonadherent bacteria and other debris from the mouth (5). Certain medications, head and neck radiation therapy, Sjögren's disease, and other systemic conditions, including DM, may reduce salivary flow. The diabetic condition associated with prolonged hyperglycemia can infer salivary gland function and influence the amount and nature of saliva produced (6). The subjective feeling of mouth dryness is known as xerostomia (7). Of the patients with DM, 10-30% exhibit xerostomia, a condition characterized by decreased saliva production (8). Hypofunction of the salivary glands can cause changes in the oral mucosa, including elevated concentrations of glucose and mucin, a reduction in the generation of antimicrobial agents, loss of taste perception, halitosis, periodontal disease, dental caries, inefficient wound healing, and a predisposition to oral mucosal disease (9). Saliva's wide range of antibacterial agents, antibodies, and buffers gives it a protective role; hence, periodontal health can deteriorate by a decrease in its flow rate (10). Given the significant burden of oral diseases and their association with DM, oral health problems contribute to pain, impaired mastication, and xerostomia, significantly impacting the overall quality of life, loss of work productivity, and high treatment costs (11,12). Nevertheless, oral health is still a neglected and underestimated health concern globally (13). Hence, the present study aimed to assess and correlate the oral health status and glycemic control level of patients with T2DM.

Methods

Study design and patient selection

In this cross-sectional study, patients who applied to the Department of Periodontics at AB Shetty Memorial Institute of Dental Sciences, Mangalore, Karnataka, underwent screening and clinical examinations between July 2022 and June 2023. Patients in the age group of 35 to 65 years, medically diagnosed with T2DM for the past five years with good glycemic control ≤7% of glycated hemoglobin (HbA1c), and poor glycemic control of >7% of HbA1c, with a minimum complement of 20 natural teeth, were included in the study (14). Patients diagnosed with any systemic illness other than T2DM and those under medication that affects the periodontium (such as antiepileptic drugs and immunosuppressants), those who underwent periodontal therapy three months before the study, smokers, and pregnant or nursing women were excluded. The study was approved by the AB Shetty Memorial Institute of Dental Sciences Institutional Ethics Committee (ref. no: ETHICS/ABSMIDS/269/2022, date: 25.06.2022) and was conducted in compliance with the principles outlined in the Helsinki Declaration, revised in 2013. Written informed consent was obtained from the participants.

Data collection

Demographic and clinical data

Standard demographic data, including age, sex, and body mass index (BMI), were collected using a standardized proforma for the participants. Glycemic control was estimated based on HbA1c values. Participants without an HbA1c report within the past three months of the study were referred to the institution's medical center for HbA1c level measurement.

Assessment of oral health

Oral and periodontal health was assessed using the following parameters: Oral hygiene status was evaluated using the full mouth plaque score (FMPS) (15). The full mouth bleeding score (FMBS), PD, and clinical attachment level (CAL) were measured with a marked periodontal probe (UNC-15 probe, Hu-Friedy, Chicago, IL, USA) (16,17). All teeth were probed at six sites: mesio-lingual, mid-lingual, disto-lingual, mesiobuccal, mid-buccal, and distobuccal. Plaque and bleeding scores were based on the absence or presence of plaque and bleeding, respectively.

Salivary flow and xerostomia assessment

The unstimulated salivary flow rate was assessed using the MST (Schirmer strips®). This strip was adapted from the Schirmer tear test commonly used by ophthalmologists. Patients were instructed to sit upright in a dental chair, swallow all saliva before the test, refrain from swallowing during the test, and rest their tongue on the hard palate. Using a cotton plier, the MST strip was held vertically with the rounded end at the floor of the mouth on either side of the lingual frenum. The wetness of saliva ascended the strip upon contact with the round end, and its distance was measured at 1, 2, and 3 min, with the readings promptly recorded. If the strip's moisture content was <25 mm after three minutes, hyposalivation was considered (18), A 10item questionnaire on the experience of xerostomia was used (19). Xerostomia is considered present if the patient responds positively to one or more of the following questions: Do you feel your mouth dry when you eat? Do you have difficulty swallowing food? Do you need to drink while eating? Do you feel like the amount of saliva in your mouth is too low most of the time? (adapted according to Fox criteria) (20,21).

Statistical Analysis

The collected data were analyzed using nMaster software version 2. For scale variables, data were expressed as mean and standard deviation, and for categorical variables, data were expressed as frequency percentages. The chi-square test was employed to compare xerostomia, hyposalivation, and periodontal status with glycemic control levels in patients with T2DM. Pearson's correlation was used to assess the correlation

between HbA1c and the clinical variables FMPS, FMBS, and CAL. P values less than 0.05 were considered statistically significant.

Results

Seventy patients with T2DM, comprising 49 males (70%) and 21 females (30%), participated in the study. The mean age of the participants was 53.7±8.3 years (males 55.3±8.3 and females 49.3±6.8 years, respectively). As shown in Table 1, the participants had a mean HbA1c level of 6.9±0.9 % among patients with T2DM. Notably, most participants exhibited good glycemic control (67.4%), with 32.8% demonstrating poor glycemic control. The mean PD and CAL were 2.8±1.5 mm and 4±1.5 mm, respectively. Over half (67.1%) of the T2DM patients exhibited good glycemic control. Gingivitis was present in 50% of the participants, and the remaining population had moderate-to-severe chronic periodontitis (41.4% and 8.6%, respectively). Xerostomia was reported in 65.7% of participants, whereas hyposalivation was present in only 20% of the population.

Among the participants with poor glycemic control, approximately 52.2% had xerostomia, whereas only one-fourth (24.5%) of participants with good glycemic control reported

Table 1. Demographic and clinical characterstudy population	istics of the		
Age, years, mean±SD			
Male	55.3±8.3		
Female	49.3±6.8		
Overall	53.7±8.3		
Sex , n (%)			
Male	49 (70)		
Female	21 (30)		
BMI, kg/m², mean±SD			
Male	25.1±5.8		
Female	23.0±4.3		
Overall	23.2±4.9		
HbA1c, %, mean±SD	6.9±0.9		
FMPS, %, mean±SD	38.7±5.3		
FMBS, %, mean±SD	20.1±6.1		
PD, mm, mean±SD	2.8±1.5		
CAL, mm, mean±SD	4±1.5		
Glycemic control, n (%)			
Good	47 (67.1)		
Poor	23 (32.8)		
Periodontal status, n (%)			
Gingivitis	35 (50)		
Moderate periodontitis	29 (41.4)		
Severe periodontitis	6 (8.6)		
Xerostomia, n (%)	24 (34.3)		
Hyposalivation, n (%)	14 (20)		
SD: Standard deviation, BMI: Body mass index, HbA1c: Glycated hemoglobin			

SD: Standard deviation, BMI: Body mass index, HbA1c: Glycated hemoglobin, FMPS: Full mouth plaque scores, FMBS: Full mouth bleeding scores, PD: Probing depth, CAL: Clinical attachment level, n: Number, %: Percentage xerostomia, and the difference was statistically significant (p=0.027). Additionally, it was observed that among the T2DM individuals with poor glycemic control, approximately 47.8% had hyposalivation, whereas among those with good control, only 6.4% exhibited hyposalivation, and the distribution was statistically significant (p=0.001). Within the group of individuals exhibiting poor glycemic control, 47.8% and 21.7% had moderate and severe periodontitis, respectively. Conversely, among participants with optimal glycemic control, 59.6% developed gingivitis, whereas only 2.1% developed severe periodontitis. This distribution was statistically significant (p=0.007) (Table 2).

Correlation of glycemic control with clinical variables

HbA1c had a moderate positive correlation with FMPS that was statistically significant (r=0.447; p=0.001) and a low degree of correlation with FMBS (r=0.283; p=0.018) and CAL (r=0.301; p=0.011), respectively (Pearson's correlation, statistically significant at p<0.01 and p<0.05).

Discussion

The sensation of having a dry mouth (xerostomia) is one of the most prevalent symptoms of DM (22). Hyperglycemia and diabetic neuropathy in uncontrolled T2DM can lead to xerostomia because excessive glucose is converted into sorbitol, damaging nerve cells and causing abnormalities in salivary secretion (23). The onset and progression of numerous symptoms and oral manifestations are significantly influenced by glucose regulation (24).

In this regard, the present study illustrated that the prevalence of xerostomia was higher in patients with T2DM who had poor glycemic control than those with good glycemic control. In support of the present study, an investigation by Shrivastava et al. (25) reported that individuals with T2DM exhibited a higher prevalence of xerostomia with increased HbA1c levels. However,

Table 2. Distribution of clinical conditions of the study participants based on the glycemic control levels				
Clinical conditions		Glycemic control		
		Good	Poor	p value
Xerostomia, n	(%)	12 (25.5)	12 (52.2)	0.027*
Hyposalivatio	n, n (%)	3 (6.4)	11 (47.8)	0.001*
Periodontal status	Gingivitis, n (%)	28 (59.6)	7 (30.4)	
	Moderate periodontitis, n (%)	18 (38.3)	11(47.8)	0.007*
	Severe periodontitis, n (%)	1 (2.1)	5 (21.7)	-
n: Number %: *Statistically significant				

contrary to the current study findings, another study revealed no significant difference in the incidence of xerostomia reported by patients with controlled and uncontrolled T1DM and T2DM (26). Several pathological alterations, including malfunction of the salivary glands and decreased salivary production, are frequently evident in hyperglycemia (27). The current investigation revealed that patients with poorly controlled T2DM exhibited a higher number of individuals experiencing hyposalivation compared with those with good control. Al-Maweri et al. (26) observed a similar pattern in participants with T1DM or T2DM, but the results were nonsignificant. Additionally, findings from another study suggest a possible association between salivary flow and composition and poor glycemic control in patients with T2DM (28). Conversely, Dodds and Dodds (19) found no noticeable differences in the salivary flow rate of patients with T2DM.

Changes in the salivary glands driven by the detrimental effects of DM can cause a decrease in saliva, which can have adverse consequences like a higher risk of developing periodontal disease and dental caries (29). Moreover, inadequate regulation of glucose levels has been identified as a significant factor contributing to periodontitis (30). The present study revealed a higher prevalence of chronic periodontitis in individuals with T2DM who exhibited inadequate glycemic control compared with those with good glycemic control. Many hypotheses have been established to explain the plausibility of uncontrolled DM and periodontal diseases, such as host response alterations, collagen metabolism, and vascularity (31). Similarly, Awartani (32) showed an increased mean CAL in individuals with poor glycemic control compared with those with good glycemic control. Hence, the negative impact of T2DM on periodontal health increases with poorer glycemic control.

Notable alterations in poorly controlled DM include diminished defense mechanism and vulnerability to infections, ultimately resulting in destructive periodontal disease (33). Elevated glucose levels in the gingival fluid and bloodstream in individuals with DM may cause qualitative shifts in bacteria, potentially worsening the severity of periodontal disease in those with poorly controlled DM (34).

In this regard, in the current study, participants with poorly controlled T2DM had a higher number of individuals with severe periodontitis than those with good glycemic control. These results align with observations from another study, in which patients with poorly controlled T2DM had a higher prevalence of severe periodontitis (2.5%) than those with normal or good glycemic control (0%) (35). However, contrary to this, a study in an Indonesian population found no correlation between any measure of periodontitis severity and HbA1c levels in individuals with T2DM. The authors outlined several factors, such as diverse medications for blood sugar control, the potential impact of BMI on insulin resistance, and ethnic variations across different study populations, for the absence of a relationship between HbA1c and periodontitis severity (36).

The current study findings corroborate those reported by Kumar et al. (2013) (37), who observed an association between good oral hygiene and lower HbA1c levels in patients with T2DM. Qureshi et al. (2020) (38) found a significant correlation between periodontal parameters and HbA1c levels in patients with T2DM, similar to the present findings. Another cross-sectional study further substantiated the findings of the current study. The study revealed that participants with T2DM and poor glycemic control exhibited higher mean plaque, bleeding, and CAL (39).

Study Limitations

The main limitation of this study is that it only included a convenience sample of patients with DM from a particular institution. Consequently, these findings may not be fully generalizable to individuals with diabetes in other geographic regions. Future longitudinal studies are warranted to explore causality and better understand the dynamics over time. Second, the questionnaire we used to determine xerostomia was subjective. Third, we were not able to evaluate socioeconomic status, including occupation and education level, the frequency of dental checkup visits, and awareness of the connections between oral and systemic diseases that determine oral health.

Conclusion

The study concluded that individuals with poor glycemic control for T2DM have a higher incidence of xerostomia, hyposalivation, and compromised periodontal health, resulting in a decline in their oral health status. These findings suggest that poor glycemic control negatively impacts oral health. More comprehensive observational studies are required to explore oral health concerns and associated factors among individuals with T2DM.

Ethics

Ethics Committee Approval: The study was approved by the AB Shetty Memorial Institute of Dental Sciences Institutional Ethics Committee (ref. no: ETHICS/ABSMIDS/269/2022, date: 25.06.2022) and was conducted in compliance with the principles outlined in the Helsinki Declaration, revised in 2013.

Informed Consent: Written consent was obtained from the participants, who were informed about the study objectives.

Authorship Contributions

Concept: B.A.K., N.S., A.S., Design: B.A.K., N.S., A.S., Data Collection or Processing: B.A.K., K.S.C., Analysis or Interpretation: B.A.K., N.S., Literature Search: B.A.K., N.S., K.S.C., Writing: B.A.K., N.S., K.S.C.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

- 1. Roden M, Shulman GI. The integrative biology of type 2 diabetes. Nature. 2019;576:51-60.
- Michalowicz BS, Hodges JS, Pihlstrom BL. Is change in probing depth a reliable predictor of change in clinical attachment loss? J Am Dent Assoc. 2013;144:171-178.
- Löe H. Periodontal disease. The sixth complication of diabetes mellitus. Diabetes Care. 1993;16:329-334.
- Jimenez M, Hu FB, Marino M, Li Y, Joshipura KJ. Type 2 diabetes mellitus and 20 year incidence of periodontitis and tooth loss. Diabetes Res Clin Pract. 2012;98:494-500.
- 5. Scannapieco FA. Saliva-bacterium interactions in oral microbial ecology. Crit Rev Oral Biol Med. 1994;5:203-248.
- von Bültzingslöwen I, Sollecito TP, Fox PC, et al. Salivary dysfunction associated with systemic diseases: systematic review and clinical management recommendations. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;103(Suppl):57.
- Villa A, Wolff A, Aframian D, et al. World Workshop on Oral Medicine VI: a systematic review of medication-induced salivary gland dysfunction: prevalence, diagnosis, and treatment. Clin Oral Investig. 2015;19:1563-1580.
- Negrato CA, Tarzia O. Buccal alterations in diabetes mellitus. Diabetol Metab Syndr. 2010;2:3.
- Chávez EM, Borrell LN, Taylor GW, Ship JA. A longitudinal analysis of salivary flow in control subjects and older adults with type 2 diabetes. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2001;91:166-173.
- Takeuchi K, Furuta M, Takeshita T, et al. Risk factors for reduced salivary flow rate in a Japanese population: the Hisayama Study. Biomed Res Int. 2015;2015:381821.
- Petersen PE, Bourgeois D, Ogawa H, Estupinan-Day S, Ndiaye C. The global burden of oral diseases and risks to oral health. Bull World Health Organ. 2005;83:661-669.
- Newton JT, Prabhu N, Robinson PG. The impact of dental appearance on the appraisal of personal characteristics. Int J Prosthodont. 2003;16:429-434.
- Rawal I, Ghosh S, Hameed SS, et al. Association between poor oral health and diabetes among Indian adult population: potential for integration with NCDs. BMC Oral Health. 2019;19:191.
- American Diabetes Association. Standards of Medical Care in Diabetes-2022 Abridged for Primary Care Providers. Clin Diabetes. 2022;40:10-38.
- O'Leary TJ, Drake RB, Naylor JE. The plaque control record. J Periodontol. 1972;43:38.
- Ainamo J, Bay I. Problems and proposals for recording gingivitis and plaque. Int Dent J. 1975;25:229-235.
- Newman MG, Takei H, Klokkevold PR, Carranza FA. Newman and Carranza's Clinical Periodontology. In: Periodontal examination and diagnosis. 13th ed. Philadelphia: Elsevier Health Sciences; 2018:387-389.
- Khovidhunkit SO, Suwantuntula T, Thaweboon S, Mitrirattanakul S, Chomkhakhai U, Khovidhunkit W. Xerostomia,

hyposalivation, and oral microbiota in type 2 diabetic patients: a preliminary study. J Med Assoc Thai. 2009;92:1220-1228.

- Dodds MW, Dodds AP. Effects of glycemic control on saliva flow rates and protein composition in non-insulin-dependent diabetes mellitus. Oral Surg Oral Med Oral Pathol Oral Radiol Endod.1997;83:465-470.
- Fox PC, Busch KA, Baum BJ. Subjective reports of xerostomia and objective measures of salivary gland performance. J Am Dent Assoc.1987;115:581-584.
- Moore PA, Guggenheimer J, Etzel KR, Weyant RJ, Orchard T. Type 1 diabetes mellitus, xerostomia, and salivary flow rates. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2001;92:281-291.
- Malicka B, Kaczmarek U, Skośkiewicz-Malinowska K. Prevalence of xerostomia and the salivary flow rate in diabetic patients. Adv Clin Exp Med. 2014;23:225-233.
- Susanto H, Agustina D, Abbas F, Vissink A. Xerostomia, glucose regulation and serum inflammatory markers in Indonesians with type 2 diabetes mellitus. Oral Surgery Oral Medicine Oral Pathology and Oral Radiology. 2015;119:e112.
- 24. Hoseini A, Mirzapour A, Bijani A, Shirzad A. Salivary flow rate and xerostomia in patients with type I and II diabetes mellitus. Electron Physician. 2017;9:5244-5249.
- Shrivastava S, Naidu GS, Makkad RS, Nagi R, Jain S. Oral health related quality of life of controlled and uncontrolled type II diabetes mellitus patients-a questionnaire based comparative study. J Dent Res. 2018;14:20-24.
- Al-Maweri SA, Altayyar MO, AlQahtani KW, et al. Xerostomia, Salivary Flow, and Oral Health Status Among Saudi Diabetic Patients: A Comparative Cross-Sectional Study. Clin Cosmet Investig Dent. 2021;13:451-458.
- Díaz Rosas CY, Cárdenas Vargas E, Castañeda-Delgado JE, Aguilera-Galaviz LA, Aceves Medina MC. Dental, periodontal and salivary conditions in diabetic children associated with metabolic control variables and nutritional plan adherence. Eur J Paediatr Dent. 2018;19:119-126.
- Puttaswamy KA, Puttabudhi JH, Raju S. Correlation between Salivary Glucose and Blood Glucose and the Implications of Salivary Factors on the Oral Health Status in Type 2 Diabetes Mellitus Patients. J Int Soc Prev Community Dent. 2017;7:28-33.
- 29. Rahiotis C, Petraki V, Mitrou P. Changes in saliva characteristics and carious status related to metabolic control in patients with type 2 diabetes mellitus. J Dent. 2021;108:103629.
- Emrich LJ, Shlossman M, Genco RJ. Periodontal disease in non-insulin-dependent diabetes mellitus. J Periodontol. 1996;62:123-131.
- Lalla E, Papapanou PN. Diabetes mellitus and periodontitis: a tale of two common interrelated diseases. Nat Rev Endocrinol. 2011;7:738-748.
- Awartani FA. Evaluation of the relationship between type 2 diabetes and periodontal disease. Saudi Med J. 2009;30:902-906.
- Ficara AJ, Levin MP, Grower MF, Kramer GD. A comparison of the glucose and protein content of gingival fluid from diabetics and nondiabetics. J Periodontal Res. 1975;10:171-175.

- 34. Iacopino AM. Periodontitis and diabetes interrelationships: role of inflammation. Ann Periodontol. 2001;6:125-137.
- Singh M, Bains VK, Jhingran R, et al. Prevalence of periodontal disease in type 2 diabetes mellitus patients: A cross-sectional study. Contemp Clin Dent. 2019;10:349-357.
- Susanto H, Nesse W, Dijkstra PU, et al. Periodontal inflamed surface area and C-reactive protein as predictors of HbA1c: a study in Indonesia. Clin Oral Investig. 2012;16:1237-1242.
- 37. Kumar A, Pandey MK, Singh A, Mittra P, Kumar P. Prevalence and severity of periodontal diseases in type 2 diabetes

mellitus of Bareilly region (India). Int J Med Sci Public Health. 2013;2:77-83.

- Qureshi A, Haque Z, Bokhari SAH, Baloch AA. Evaluation of HbA1c in type-2 diabetes mellitus patients with periodontitis: preliminary findings of three-arm clinical trial. J Pak Med Assoc. 2020;70:1350-1356.
- Stoicescu M, Calniceanu H, Ţig I, et al. Significant aspects and correlation between glycemic control and generalized chronic periodontitis in type 2 diabetes mellitus patients. Exp Ther Med. 2021;22:671.