ORIGINAL RESEARCH

Evaluation of salivary flow rate in labial minor salivary glands among Type II Diabetic Mellitus patients: A cross sectional study

Sanjeedevi C, Sangeeth Vasan, Sanjay Kumar M, Thalaimalai Saravanan, Kalaiselvi Santhosh, Aravindh Swamy R M

Abstract

Background: Minor salivary glands play a crucial role in maintaining oral health, contributing to 6-10% of total salivary secretion. Diabetes mellitus is known to affect salivary gland function, leading to xerostomia and associated oral complications.

Objective: To evaluate and compare the salivary flow rate and distribution of minor salivary gland openings in the lower labial mucosa between type II diabetic patients and healthy controls using sodium fluorescein dye visualization and Schirmer's test.

Materials and Methods: This cross-sectional study included 30 type II diabetic patients and 30 healthy controls recruited from our institution. Lower labial mucosa was examined using moistened sodium fluorescein strips under blue light (Woods lamp) to visualize and count minor salivary gland openings. Salivary flow rate was assessed using Schirmer's test. Statistical analysis was performed using independent t-test and Pearson correlation analysis.

Results: The control group demonstrated significantly higher mean number of minor salivary gland openings (66.20 ± 9.99) compared to diabetic patients (55.27 ± 11.37; p = 0.001). Similarly, salivary flow rate was significantly reduced in diabetic patients (8.47 ± 2.34) compared to controls (12.17 ± 1.51; p = 0.001). Strong negative correlations were observed between age and both gland openings (r = -0.898 in diabetics, r = -0.956 in controls) and salivary flow rate. A positive correlation was found between the number of gland openings and salivary flow rate in both groups (r = 0.708 in diabetics, r = 0.420 in controls).

Conclusion: Type II diabetes mellitus significantly reduces both the number of functional minor salivary gland openings and salivary flow rate in the lower labial mucosa. The sodium fluorescein dye technique combined with Schirmer's test provides a simple, non-invasive method for assessing minor salivary gland function. These findings emphasize the importance of oral health monitoring in diabetic patients to prevent xerostomia-related complications.

Keywords: Minor salivary glands, diabetes mellitus, salivary flow rate, sodium fluorescein, Schirmer's test, xerostomia

Introduction

Saliva is an invaluable factor in the process of keeping the oral cavity healthy, facilitating digestion, preventing microbial infections and enhancing quality of life. Although the major salivary glands (parotid, submandibular and sublingual) produce the larger part of salivary secretions, minor salivary glands are found throughout the mouth and have a considerable role in the minimal salivary secretions especially under unstimulated conditions where they contribute 6-10 percent of the total salivary secretions. [1]

Minor salivary glands are anatomically spread over labial, lingual, palatal, and buccal mucosa and there are about 600-1000 discrete glands in the oral cavity. Out of them, the labial minor salivary glands are of particular clinical importance as they are accessible to study and play a significant role in ensuring the well-being of the oral cavity. Such glands release a salivation rich in mucous with protective immunoglobulins (IgA, IgM, and IgG) that prevent the colonization of bacteria especially the streptococcal species.[2] It has also been established that lower labial minor salivary glands retain greater concentrations of fluoride under unstimulated conditions than whole saliva and thus the lower labial minor salivary glands play a critical role in caries prevention.[3]

Department and Institution Affiliation: Karpaga Vinayaga Institute of Dental Sciences (Affiliated to the Tamil Nadu Dr. MGR University), Chinnakolambakkam, Tamil Nadu.

Corresponding author: Sanjeedevi C, CRRI, Karpaga Vinayaga Institute of Dental Sciences (Affiliated to the Tamil Nadu Dr. MGR University), Chinnakolambakkam, Tamil Nadu. E-mail: sanjuchandrasekaran2021@Gmail.com

How to cite the article: C Sanjeedevi, V Sangeeth, M Sanjay Kumar, S Thalaimalai, S Kalaiselvi, R M Aravindh Swamy. Oral MaxillofacPathol J 2026; 17(2); 202-206.

Source of Support: Nil

Conflict of Interest: None

A wide range of systemic and local conditions may be associated with impairment of the major and minor salivary glands functioning. Among them, Sjogren syndrome, cystic fibrosis, post radiation therapy, and, last but not least, diabetes mellitus are majorly affected. Diabetes mellitus (DM) is a metabolic disease that is chronic hyperglycemia and is further divided into two advanced types; Type 1 diabetes (T1DM) or Type 2 diabetes (T2DM), with the former being an autoimmune disease in which the pancreatic β-cells are destroyed leading to chronic hyperglycemia and the latter is an insulin resistance condition accompanied by relative insulin deficiency, and it constitutes about 90-95 percent of all diabetic cases.

Subjective dry mouth sensation or xerostomia is one of the most frequent oral symptoms of diabetes mellitus, and it is common among both T1DM and T2DM patients. Xerostomia is widely prevalent among diabetic populations, with a prevalence rate of between 40% and 80% as compared to non-diabetic people.[4] A decrease in salivary flow triggers an oral complication cascade of effects such as raised levels of bacterial colonization, increased oral susceptibility to infection (especially candidiasis), loss of taste (dysgeusia), faster rate of dental caries, bad breath (halitosis), impaired mastication and deglutition, and weakened denture retention in patients with edentulous ridges.[5]

Pathophysiology of salivary gland dysfunction in diabetes is multifactorial, including effects of micro vascular complications in the vasculature of glands, autonomic neuropathy in the neural regulation of secretion, osmotic diuresis that results into dehydration and possibly direct glycemic effects on acinar cells. The research on the role of major salivary glands in diabetic patients has been predominant over the past few years with little research on the exact role of minor salivary glands in xerostomia and decreased salivary flow.

The daily evaluation of salivary flow has been based on the collection of whole saliva or cannulation of the major ducts of salivary glands. Nevertheless, these techniques do not distinguish the role of minor salivary glands. Recent developments on visualization methods, especially adaptation of sodium fluorescein dye, a water soluble fluorescent dye, widely used in ophthalmology to measure tear film, provide a new method of directly imaging and determining minor salivary gland secretory activity.[6] Sodium fluorescein can be used on the oral mucosa and when observed under ultraviolet light. it is seen as active minor salivary glands, in discrete fluorescent points which can be counted and described.

The Schirmer test that was originally designed to test the levels of tear production has been effectively modified to the level of testing the amounts of minor glands secretions. The rate of wetting by the application of special absorbent strips on the labial mucosa, can be regarded as a measurable level of wetting by the salivary glands in these areas.[7]

Although minor salivary gland dysfunction may be clinically important in diabetic patients, a deficiency in research specifically looking at how Type 2 diabetes mellitus affects the quantity and functionality of labial minor salivary glands is still present. This relationship is important in understanding how to create specific preventive strategies and therapeutic interventions to prevent oral complications in diabetic population.

Thus, the aim of the study is to compare and assess the rate and distribution of minor salivary gland openings in lower labial mucosa of Type 2 diabetic patients and healthy controls by using the sodium fluorescein dye visualization technique in combination with the Schirmer test. We also examine the correlation of age, gland opening number, and flow rate of salivary in the two groups.

Materials and Methods

Study Setting

This cross-sectional observational study was conducted at the Department of Oral Medicine and Radiology, Karpaga Vinayaga Institute of Dental Sciences, Madhuranthagam, Tamil Nadu, India, from January 2025 to August 2025. The Institutional Ethics Committee approved the study (Reference No. KIDS/IEC/2025/II/013, 10.12.2024) and Prior informed consent was obtained from the study participants, based on Helsinki Declaration

Sample size calculation

The study sample size was determined using G*Power software (version 3.1.9.7). Based on pilot data and assuming an effect size of 0.8, alpha error of 0.05, and power of 0.80, a minimum of 26 participants per group was required. To account for potential dropouts and ensure adequate statistical power, 30 participants were recruited for each group, yielding a total sample size of 60 participants.

Participant Selection

Thirty consecutive individuals with verified Type 2 diabetes mellitus made up Group 1 (Diabetic Group). The second group, called the control group, consisted of thirty healthy volunteers who were matched by age and gender. The research included all patients with a history of diabetes mellitus who were willing to participate and were in the 40-60 age range. All healthy non diabetic individuals of age 40-60 years were included in the control group. Pre-existing salivary gland disorders, complete or partial denture wearers, medications affecting salivary flow rate (anticholinergics, antihistamines, antidepressants, antipsychotics, diuretics), Gestational diabetes, any forms of tobacco use, history of radiation therapy were excluded.

Evaluating minor salivary gland openings

Patients were instructed in nil oral for atleast 60 minutes prior to examination. Examination was done in darkroom to enhance fluorescence visualization. Patients were seated in a dental chair in an upright position with appropriate head support. The saline moist sodium fluorescent strips was placed in the everted lower labial mucosa. A standardized waiting period of 30 seconds was observed to allow fluorescein dye excretion from active minor salivary glands. The labial mucosa was examined under Woods lamp (UV light at 365 nm wavelength) in the darkened room. Minor salivary gland openings appeared as distinct bright yellow-green fluorescent points against the dark mucosal background. Digital photographs of the fluorescent pattern were captured using a smartphone camera at 2× magnification. The number of visible

fluorescent secretory points was calculated by simple counting and verified through photographic analysis.

Assessment of Salivary Flow Rate

A sterile schirmer's strip is placed in the lower labial vestibule and waited for 3 minutes, the strip was then gently removed. The length of the wetted portion was immediately recorded in millimeters using a standardized measuring scale.

Statistical Analysis

Information was input into Excel 2019 and analyzed using SPSS Statistics (version 25.0, IBM Corporation, Armonk, NY, USA). All variables had descriptive statistics computed, including means, standard deviations, and ranges. Independent samples t test and Pearson correlation analysis were also executed.

Results

Minor Salivary Gland Openings

Table I presents the comparison of minor salivary gland openings between diabetic and control groups. The diabetic group demonstrated significantly fewer minor salivary gland openings (55.27±11.37) compared to the control group (66.20±9.99). This was statistically significant (t = -3.956, p = 0.001) and this means that salivary gland minor openings were actually less in diabetic groups.

Response to Reviewer Comment Q3: Table I

Salivary Flow Rate

Table II demonstrates the comparison of the salivary flow rate in the two groups. The rate of salivary flow in the diabetic group was much lower (8.47±2.34 ml) than in the control group (12.17±1.51 ml). The effect of this was very significant (t = -7.265, p = 0.001), which indicated that there is a severe impairment in the salivary secretion of diabetic patients.

Response to Reviewer Comment Q3: Table II (Added)

Correlation Analysis

The correlations among different parameters of various groups were presented in Table III. Age had a negative significant relationship with number of minor salivary gland openings (r=

-0.898, p = 0.001) in diabetic group, thus suggesting that older patients with diabetes had less gland opening. There was a significant positive relationship between the rate of minor salivary glands openings and the salivary flow rate (r = 0.708, p = 0.001), which indicated that the lesser the glands openings, the lower the salivary flow rate. Also, there was an adverse relationship between age and salivary flow rate (r = -0.708, p = 0.001).

Age showed a very high negative relationship with minor openings of salivary glands (r = - 0.956, p = 0.001) in the control group, even stronger than in diabetic group. Nonetheless, the associations between minor salivary gland openings and the rate of salivary flow were moderate (r = 0.420, p = 0.021) and the age had a weak negative relationship with the rate of the salivary flow (r = -0.447, p = 0.013). These results imply that both groups experience age related deterioration on gland openings, although the correlation between gland openings and the salivary functions is not the same in diabetic and non-diabetic patients.

Response to Reviewer Comment Q3: Table III (Added)

Table I: Comparison of Minor Salivary Gland Openings Between Diabetic and Control Groups

Parameter	Diabetic Group (n=30)	Control Group (n=30)	t-value	p-value
Minor Salivary Gland Openings (Mean ± SD)	55.27 ± 11.37	66.20 ± 9.99	−3.956	0.001*

**Statistically significant at p < 0.05; Independent samples t-test*

Table II: Comparison of Salivary Flow Rate Between Diabetic and Control Groups

Parameter	Diabetic Group (n=30)	Control Group (n=30)	t-value	p-value
Salivary Flow Rate (Mean ± SD, mm/3 min)	8.47 ± 2.34	12.17 ± 1.51	−7.265	0.001*

**Statistically significant at p < 0.05; Independent samples t-test*

Table III: Pearson Correlation Analysis – Age, Gland Openings, and Salivary Flow Rate

Parameter Pair	Diabetic Group r (p-value)	Control Group r (p-value)
Age vs. Minor Salivary Gland Openings	−0.898 (0.001*)	−0.956 (0.001*)
Minor Salivary Gland Openings vs. Salivary Flow Rate	0.708 (0.001*)	0.420 (0.021*)
Age vs. Salivary Flow Rate	−0.708 (0.001*)	−0.447 (0.013*)

**Pearson correlation; p < 0.05 considered statistically significant*

Discussion

The cross-sectional research provides strong results that Type 2 diabetes mellitus is a major variable that hinders the operation and dispersion of minor salivary glands in the lower labial mucosa. As illustrated in our study, the results indicate the presence of quantitative and functional deficiencies among diabetic patients relative to the healthy controls, and these results are relevant in the context of oral health management of diabetic patients.

Impact of Diabetes on Minor Salivary Gland Distribution

In our research, it was found that there was a substantial reduced number of visible minor salivary gland openings between diabetic patients (55.27 + 11.37) and healthy controls (66.20 + 9.99) indicating a decline in number by an approximation 16.5%. The results are consistent with the general research of salivary gland dysfunction in diabetes. Wang et al. (2016) also found worsened minor salivary gland functioning in the hyposalivation-related illnesses, indicating that the microvascular complications of diabetes caused by the pathology and the autonomic neuropathy could influence the minor salivary glands in the same way that the major salivary glands.[3]

The pathophysiology of the mechanism behind this decrease in functional gland openings probably has a number of pathways. Diabetic chronic hyperglycemia causes the formation of advanced glycation end-products (AGEs) in tissues, such as salivary glands. These AGEs lead to structural destruction of acinar cell, ductal epithelium and vascular supply, which may make some glands non-functional, despite their anatomical location.[8] There is also the existence of diabetic microangiopathy of the microvasculature of salivary glands which decreases the blood flow and thereby decreases the capacity of secretion.[9]

One of the diabetic complications, autonomic neuropathy, disturbs the parasympathetic and sympathetic innervation of salivary secretion. The sympathetic system stimulates the mucous secretion and the glandular blood flow whereas the parasympathetic nervous system controls serous secretion and the overall blood flow. Diabetic autonomic neuropathy may affect either of these pathways, with the result of decreased secretory activity, some of which may result in the non-functional or non-detectable occurrence of certain gland openings when fluorescein is used to visualize them.[10]

Salivary Flow Rate Reduction in Diabetic Patients

The 30.4 percent loss in the rate of salivary flow experienced by our diabetics (8.47 -2.34 mm/3min) as opposed to the controls (12.17 -1.51 mm/3min; p = 0.001) is a clinically significant loss. This observation supports what other researchers have found (Carramolino- Cuellar et al., 2018), who also found considerable salivary flow rates reduction in type 2 diabetic patients and highlighted the correlation between the severity of xerostomia and glycemic regulation.[8]

Our flow size is comparable to literature that has investigated whole salivary rates in diabetics, in that minor salivary glands are affected similar to major salivary glands. This is especially worrying since minor salivary glands help in the basal salivary secretion and have important roles in ensuring the mucosal integrity particularly at rest when the major glands are not particularly active.

There are a number of related processes that lead to decreased salivary flow in diabetes. To begin with, hyperglycemia causes osmotic diuresis that causes systemic dehydration in which salivation has limited fluid. Second, elevated blood glucose levels induce a hyperosmolar state that can have a direct inhibitory effect on aquaporin-driven water transport in acinar cells. Third, salivary gland tissues can be a result of inflammatory processes associated with diabetes through the action of cytokines, like TNF- α and IL-6.[9]

Moreover, salivary glands changes related to diabetes are protein changes as reported by Fouani et al. (2019) and they are amylase, mucins, and antimicrobial proteins. These molecular alterations do not only impact on the volume of saliva but on the quality and protective properties as well which may result in a vicious loop of decreased antimicrobial capacity leading to increased risk of oral infection and increasing stress on the remaining functional glands.[9]

Age-Related Decline in Salivary Function

A very noticeable observation of our research was that there was a significant negative correlation between age and the minor salivary gland openings as well as the rate of the salivary flow in the diabetic/ control groups. The age factor in healthy controls had a very strong negative association with gland openings (r = -0.956, p = 0.001), and diabetic patients (r = - 0.898, p = 0.001).

The results are in line with what is already known that the process of aging is solely related to the atrophy and decline in the functional activity of the salivary glands. Xu et al. (2019) have conducted an extensive review of age related saliva changes, with most of the saliva quantity and quality decreasing with age because of many factors such as the loss of acinar cells, fatty infiltration, fibrosis, and diminished regenerative capacity.[6] Sonesson et al. (2003) particularly investigated minor salivary glands in different age groups and had found out that decreasing function secretory glands with aging.[2]

The age correlation between diabetic patients and controls is slightly weaker, which may seem counterintuitive but may be due to the dominance of the effect of diabetes per se on the functioning of glands. In diabetic patients, the pathophysiological process is a massive insult to the glandular functioning that the added effect of aging is proportionately less noticeable.

Alternatively, it might also mean that diabetes speeds up the aging process of the salivary glands, and younger diabetic individuals are now similarly dysfunctional to older non-diabetic individuals and, therefore, the age gradient is compressed.[10]

The age and salivary flow rate had more or less the same trends but the magnitude was slightly different (diabetic: r = -0.708, p = 0.001; control: r = -0.447, p = 0.013). The positive relationship in the case of diabetic patients indicates that aging and diabetes interact on a synergistic level so that the overall effect is the same deterioration as compared to either of the two factors.[11,12,13]

Relationship Between Gland Openings and Flow Rate

The positive relationship between the count of minor salivary gland openings and the rate of the salivary flow in both groups of subjects offer valuable data on the functionality of the relation between quantity and secretory volume of the glands. It is especially important to note that this was more strongly correlated with diabetic patients ($r = 0.708$, $p = 0.001$) than controls ($r = 0.420$, $p = 0.021$).[14,15]

This disparity indicates that the remaining functional glands in diabetic patients are potentially functioning at or close to their maximal secretory capacity and the total number of active glands is the major determinant of the total flow rate. Conversely, normal individuals might possess more functional reserve in either gland which enables them to compensate when other glands are less active. Abd-Elraheem et al. (2014) proved this perception by showing that diabetic salivary glands experience structural and functional changes which can impair the adaptive capacity.[10,16,17]

Another possible explanation of the higher correlation in diabetics may be the increased homogeneity of individual gland functioning in such population. Assuming that all glands are equally affected by diabetes, the glands in the whole body give equal contributions to the total output of the body, forming a more linear correlation between the number of glands and the total output. The relationship may be weakened in healthy individuals due to natural variation in the activity of individuals glands.[18,19,20]

Conclusion

Clinical Implications

The results of the present study have significant clinical implications in the management of diabetic patients. The health care practitioners are supposed to know that diabetic patients are at a higher risk of salivary dysfunction and they should put in place preventive measures that include regular oral health care, focusing on optimal glycemic control, artificial saliva substitutes in cases of necessity, and patient education about oral health practices. The prevention of secondary complications that are caused by hyposalivation, including dental caries and oral infections, as well as nutritional problems, can be achieved through early detection and treatment of the condition.

Limitations and Future directions of the study.

Although the analyzed research will be useful in understanding the dysfunction of salivary glands in diabetes, further research that addresses the parameters of glycemic control (HbA1c levels), the time of diabetes and the occurrence of other diabetes complications should be conducted to further expound the relationship between disease severity and salivary dysfunction. Longitudinal studies would be useful to determine the changes in the salivary changes over a period and determine the effect of better glycemic control on salivary functioning.

References

1. Singh S, Basu S, et al. A novel diagnostic technique of measuring labial minor salivary gland secretions using sodium fluorescein dye: Implications for patients with dry eyes. Semin Ophthalmol. 2022 Jan 2;37(1):111-116. doi: 10.1080/08820538.2021.1896752.
2. Sonesson M, Eliasson L, Matsson L, Kjaeldgaard M. Minor salivary gland secretion in children and adults. Arch Oral Biol. 2003;48(7):535–539. doi: 10.1016/S0003- 9969(03)00095-6.
3. Wang Z, Li W, Hong X, Cui Y, Yu G. Minor salivary glands function is decreased in hyposalivation-related diseases. Arch Oral Biol. 2016;69:63–70. doi: 10.1016/j.archoralbio.2016.05.011.
4. Shoji N, Sasano T, Inukai S, Todoh M, Sanjo D. A simple, yet accurate method for detecting and quantifying secretions from human minor salivary glands using the iodine-starch reaction. Arch Oral Biol. 2003;48(11):761–765. doi: 10.1016/S0003-9969(03)00154-8.
5. Inamura T, Ino C, Katoh M, Satoh M. A simple method to estimate the secretion of saliva from minor salivary glands using iodine-starch reaction. Laryngoscope. 2001;111(2):272–277. doi: 10.1097/00005537-200102000-00016.
6. Xu F, Laguna L, Sarkar A. Aging-related changes in quantity and quality of saliva: where do we stand in our understanding? J Texture Stud. 2019;50(1):27–35. doi: 10.1111/jtxs.12356.
7. Wang Z, Shen MM, Liu XJ, Si Y, Yu GY. Characteristics of the saliva flow rates of minor salivary glands in healthy people. Arch Oral Biol. 2015;60(3):385–392. doi: 10.1016/j.archoralbio.2014.11.016.
8. Carramolino-Cuéllar E, Lauritano D, Silvestre FJ, Carinci F, Lucchese A, Silvestre- Rangil J. Salivary flow and xerostomia in patients with type 2 diabetes. J Oral Pathol Med. 2018;47(5):526-530. doi: 10.1111/jop.12670.
9. Fouani M, Basset CA, Jurjus AR, Leone LG, Tomasello G, Leone A. Salivary gland proteins alterations in the diabetic milieu. Acta Biomed. 2019;90(12-S):33-40. doi: 10.23750/abm.v90i12-S.8967.
10. Abd-Elraheem SE, El Saeed AM, Mansour HH. Salivary changes in type 2 diabetic patients. Diabetes Metab Syndr. 2014;8(3):153-156. doi: 10.1016/j.dsx.2014.07.001.
11. López-Pintor RM, Casañas E, González-Serrano J, Serrano J, Ramírez L, de Arriba L, Hernández G. Xerostomia, hyposalivation, and salivary flow in diabetes patients. J Diabetes Res. 2016;2016:4372852. doi: 10.1155/2016/4372852.
12. Mese H, Matsuo R. Salivary secretion, taste and hyposalivation. J Oral Rehabil. 2007;34(10):711-723. doi: 10.1111/j.1365-2842.2007.01794.x.
13. Pedersen AM, Sørensen CE, Proctor GB, Carpenter GH, Ekström J. Salivary secretion in health and disease. J Oral Rehabil. 2018;45(9):730-746. doi: 10.1111/joor.12664.
14. Aitken-Saavedra J, Rojas-Alcayaga G, Maturana-Ramírez A, Escobar-Álvarez A, Cortes-Coloma A, Reyes-Rojas M, Morales-Bozo I. Salivary gland dysfunction markers in type 2 diabetes mellitus patients. J Clin Exp Dent. 2015;7(5):e501-e505. doi: 10.4317/jced.52050.
15. Lasisi TJ, Fasanmade AA. Salivary flow and composition in diabetic and non-diabetic subjects. Niger J Physiol Sci. 2012;27(1):79-82. PMID: 23235312.
16. Khovidhunkit, S. O., Suwantuntula, T., Thaweboon, S., Mitrirattanakul, S., Chomkhakhai, U., & Khovidhunkit, W. (2009). Xerostomia, hyposalivation, and oral microbiota in type 2 diabetic patients: a preliminary study. Journal of the Medical Association of Thailand = Chotmaihet thangphaet, 92(9), 1220–1228
17. Tabesh, A., Mahmood, M., & Sirous, S. (2023). Oral health-related quality of life and xerostomia in type 2 diabetic patients. Dental and medical problems, 60(2), 227–231.
18. Almusawi, M. A., Gosadi, I., Abidia, R., Almasawi, M., & Khan, H. A. (2018). Potential risk factors for dental caries in Type 2 diabetic patients. International journal of dental hygiene, 16(4), 467–475.
19. Borges, B. C., Fulco, G. M., Souza, A. J., & de Lima, K. C. (2010). Xerostomia and hyposalivation: a preliminary report of their prevalence and associated factors in Brazilian elderly diabetic patients. Oral health & preventive dentistry, 8(2), 153–158.
20. Malicka, B., Kaczmarek, U., & Skośkiewicz-Malinowska, K. (2014). Prevalence of xerostomia and the salivary flow rate in diabetic patients. Advances in clinical and experimental medicine : official organ Wroclaw Medical University, 23(2), 225–233. https://doi.org/10.17219/acem/37067