Original Article

Salivary glucose levels in Type 2 diabetes mellitus: A tool for monitoring glycemic control

B. Kartheeki, Abhishek Singh Nayyar, A. Ravikiran[1], Y. Samatha[1], K.V. Chalapathi[2], M. Prasanthi[3], K. Srikanth[4]

Department of Oral Medicine and Radiology, Saraswati-Dhanwantari Dental College and Hospital and Post-Graduate Research Institute, Parbhani, Maharashtra, [1]Department of Oral Medicine and Radiology, Sibar Institute of Dental Sciences, Guntur, [2]Department of Oral Pathology and Microbiology, KLR's Lenora Institute of Dental Sciences, Rajahmundry, [3]Department of Biochemistry, Asram Medical College, Eluru, [4]Department of Endocrinology, Endolife Hospital, Guntur, Andhra Pradesh, India

Abstract

Background and Aim of the Study: Diabetes mellitus (DM) requires a frequent monitoring of sera glucose levels in the body. This requirement of multiple pricking at regular intervals for monitoring sera glucose levels in the body is physically and psychologically traumatic to the patient. This necessitates a noninvasive procedure like salivary glucose estimation. The aim of this study was to assess whether salivary glucose levels can be used as a means of regular monitoring of DM without the need for serial invasive procedure required for sera glucose level estimations.

Subjects and Methods: The study group comprised 300 patients, divided into three sub-groups: Group 1 (healthy controls/nondiabetic patients; $n = 50$); Group 2 (controlled diabetic patients; $n = 125$); and Group 3 (uncontrolled diabetic patients; $n = 125$). After explaining the need for the study and obtaining consent, salivary sample collection was performed in the morning hours between 9.00 a.m. and 11.00 a.m. immediately after obtainment of the sera samples. Salivary and sera glucose levels were measured using glucose oxidase method.

Statistical Analysis Performed: Statistical analysis was performed with the Statistical Package for the Social Sciences version 16 software. The difference between means and standard deviations (SDs) between the groups were assessed using ANOVA one-way test, whereas multiple comparisons between different groups were carried out using Tukey's honest significant difference test. The value of $P < 0.05$ was considered statistically significant and a value <0.01 was considered highly statistically significant.

Results: In this study, salivary glucose levels increased with sera glucose levels with the correlation coefficient between sera and unstimulated salivary glucose levels in the controls being 0.517, in controlled diabetics being 0.470 and in uncontrolled diabetics being 0.498 ($P < 0.05$).

Conclusion: It was concluded from this study that saliva can be used as a potential tool in the regular monitoring of DM.

Keywords: Controlled diabetics, diabetes mellitus, uncontrolled diabetics

Address for correspondence: Dr. Abhishek Singh Nayyar, 44, Behind Singla Nursing Home, New Friends' Colony, Model Town, Panipat - 132 103, Haryana, India.
E-mail: singhabhishekndls@gmail.com

Access this article online	
Quick Response Code:	Website: www.ijcpc.org
	DOI: 10.4103/ijcpc.ijcpc_3_16

How to cite this article: Kartheeki B, Nayyar AS, Ravikiran A, Samatha Y, Chalapathi KV, Prasanthi M, *et al*. Salivary glucose levels in Type 2 diabetes mellitus: A tool for monitoring glycemic control. Int J Clinicopathol Correl 2017;1:7-14.

INTRODUCTION

The term diabetes was probably coined by Apollonius of Memphis around 250 B.C., which literally meant to go through or siphon as the disease drained more fluid than a person could consume. Sometimes later, the Latin word mellitus was added because it made the urine sweet.[1] Type 2 diabetes mellitus (DM) is more common representing about 80%–93% of the total number of patients affected by this complex metabolic disorder often arising in the middle to late life. Type 2 DM frequently remains undiagnosed for many years as in the early stages of the disease process, hyperglycemia develops gradually.[2] Currently, sera glucose levels are used for diagnosis and monitoring control of the disease process. However, collection of serum for measuring glucose has its own disadvantages including it being an invasive procedure, being painful and the risk of transmission of infectious disease processes in cases where a strict asepsis in not followed. Thus, a simpler screening criterion which is noninvasive is an absolute necessity to make case finding easier for the clinicians and for the frequent monitoring of the disease. Furthermore, the ability to monitor health status, disease onset, progression, and treatment outcome through noninvasive means is a highly desirable goal in health care management.[3] Like serum, saliva is a complex biological adjunct containing a variety of hormones, antibodies, enzymes, anti-microbial, and growth factors. Many of these enter saliva from the serum by passing through the spaces between the cells by transcellular (passive intracellular diffusion and/or active transport) or para-cellular (extra-cellular ultra-filtration) routes. Therefore, most of the components found in the serum are also present in saliva, thus, making saliva functionally equivalent to serum in reflecting the physiological status of the body, including the hormonal, nutritional, and various metabolic variations.[4] The pace of research in relation to the salivary diagnostics and proteomics, however, could not reach the extent that was expected with the advent of newer techniques in the recent decades. The major problems in clinical salivary diagnostics are attributed mainly due to nonstandardized collection procedures and difficulty in interpretations caused due to the great diurnal variations of salivary secretion and the individual differences, in general. The major advantages of using saliva as a diagnostic fluid are its noninvasiveness, ease of collection, no requirement of special equipment and/or trained staff, its usefulness in blood dyscrasias along with a likely better compliance with the children and geriatric patients. Many studies conducted in the past have showed a positive correlation between salivary and sera glucose levels in the Western populace and have suggested that salivary glucose levels can be used as a potentially useful, noninvasive tool in monitoring the glycemic control in diabetic patients. The present study was, therefore, conducted with an aim to ascertain if a similar correlation exists in the Indian subjects, wherein DM is becoming a force to reckon with. The studies performed on the salivary composition of diabetic patients are very few, particularly in India. Further, the results reported, so far, were contradictory in several aspects and this suggested the need for further investigative studies. The aim of the present study, therefore, was to assess the potential of saliva as a diagnostic tool for monitoring DM. The objectives of the study were to estimate salivary and sera glucose levels in controlled and uncontrolled diabetic groups and healthy controls; to correlate salivary and sera glucose levels in controlled and uncontrolled diabetic groups and healthy controls; to correlate salivary and sera glucose levels in controlled and uncontrolled diabetic groups; and to assess if salivary glucose levels can be used as a potentially useful, noninvasive tool in the regular monitoring of DM.

SUBJECTS AND METHODS

Source of data: The present study was carried out in the Department of Oral Medicine and Radiology.

The method of collection of data: The study group comprised 300 subjects, divided into three sub-groups including:

- Group 1: (Healthy controls/nondiabetic subjects; $n = 50$)
- Group 2: (Controlled diabetic subjects; $n = 125$); and
- Group 3: (Uncontrolled diabetic subjects; $n = 125$).

The following patients were excluded from the study:

- Patients with other systemic illnesses/diseases
- Pregnant females
- Smokers and alcoholics
- Persons treated with radiotherapy in the head and neck region
- Patients on drugs supposed to have an impact on the glycemic status of the patients.

The inclusion criteria were as per the current specifications (2016) of the American Diabetic Association (ADA) for diagnosis and monitoring control of the disease process in DM patients.

The study protocol was approved by the Institutional Ethics Committee. The details and the need for the study were explained to the subjects and informed consent obtained. A detailed case history was taken followed by a general and oral examination. Salivary sample collection was performed

in the morning hours between 9.00 a.m. and 11.00 a.m. immediately after obtainment of the sera samples. The samples were then processed. Salivary and sera glucose levels were measured using glucose oxidase method in Erba Chem 7, semi-automated analyzer.

Collection of sera samples

The subjects were made to sit comfortably on a chair with arms extended straight from the shoulders. The antecubital fossa was exposed and a tourniquet was applied about 1.5–2 inches above the fossa. The area was rendered aseptic with cotton wool soaked in methylated spirit. Using a 2 ml sterile, disposable plastic syringe and a 24-gauge needle, the antecubital vein was punctured and 2 ml of whole blood was drawn. The tourniquet was relieved. Cotton wool soaked with spirit was applied on the needle puncture site after the needle was removed. Serum was collected into ethylenediaminetetraacetic acid containing tube.

Procedure

The sample was centrifuged at 3000 rpm for about 5 min. One milliliter of glucose reagent was added to 10 μl of test sample and glucose standard. Both were incubated at 37°C for about 10 min. The absorbance values were measured on Erba Chem 7, semi-automated analyzer.

Collection of saliva

Spit technique was used to collect the unstimulated salivary samples. Salivary sample collection was performed in the morning between 9.00 a.m. and 11.00 a.m. immediately after obtainment of the sera samples. Patients were asked not to eat, drink, or smoke 2 h before salivary collection. The patients were asked to sit in the dental chair with head tilted forward and instructed not to speak, swallow, or do any head movements during collection of the sample. The patients were then instructed to spit the saliva into a sterile graduated container every minute for about 10 min. Saliva of about 2 ml was collected.

Procedure

The sample was centrifuged at 3000 rpm for about 20 min and clear supernatants were processed immediately for estimation of salivary levels glucose, amylase, and total protein. The test sample (100 μl) was mixed with the glucose reagent in a ratio of 1:3 and glucose standard and incubated at 37°C for 5 min. The absorbance values were measured on Erba Chem 7, semi-automated analyzer.

Calculation: Total Glucose concentration (mg/dl)

$$= \frac{\text{Absorbance of test sample}}{\text{Absorbance of standard}} \times 100$$

Statistical analysis performed

Statistical analysis was performed with the Statistical Package for the Social Sciences version 16 software (SPSS Inc., Chicago, USA). Means and standard deviations (SDs) were calculated for the individual groups. The difference between means and SDs between the groups were assessed using ANOVA one-way test, whereas multiple comparisons between different groups were done using Tukey's honest significant difference (HSD) test. Karl Pearson's correlation coefficient test was used to attain *R* - values. $P < 0.05$ was considered statistically significant and a value <0.01 was considered highly significant.

RESULTS

The study comprised 300 subjects, divided into three groups: The control group consisting of 50 subjects and the controlled and uncontrolled diabetic groups, each consisting of 125 patients. In the control group, the sera glucose levels ranged from 83 to 117 mg/dl with a mean of 99.58 mg/dl and SD of 10.59 [Table 1a], whereas the salivary glucose levels ranged from 0.70 to 1.7 mg/dl with a mean of 1.2 mg/dl and SD of 0.27 [Table 2a]. The correlation coefficient between sera and salivary glucose levels revealed an $R = 0.517$ which was found to

Table 1a: Descriptive statistics for serum glucose values

Serum glucose value	Mean	SD	SE	95% CI for mean		Minimum	Maximum
				Lower bound	Upper bound		
Control group	99.58	10.59	1.50	96.57	102.59	83.00	117.00
Controlled diabetic group	171.10	20.93	1.87	167.40	174.81	132.00	210.00
Un-controlled diabetic group	352.61	80.39	7.19	338.38	366.84	213.00	490.00
Total	234.81	115.91	6.69	221.64	247.98	83.00	490.00

CI: Confidence interval, SD: Standard deviation, SE: Standard error

Table 1b: Mean comparisons between groups using ANOVA one-way test

Source of variation	Sum of squares	df	Mean square	*F*	*P*
Between groups	3,156,210.550	2.000	1,578,105.275	544.277	<0.001 (significant)
Within groups	861,137.620	297.000	2899.453		
Total	4,017,348.170	299.000			

Statistical analysis: ANOVA one-way test. Statistically significant if $P<0.05$

Table 1c: Multiple comparisons between groups using Tukey's honest significant difference test

Group (I)	Group (J)	Mean difference (I–J)	SE	*P*	95% CI for mean	
					Lower bound	Upper bound
Control group	Controlled diabetic group	−71.52	9.010	<0.001	−92.748	−50.300
	Un-controlled diabetic group	−253.03	9.010	<0.001	−274.252	−231.804
Controlled diabetic group	Control group	71.52	9.010	<0.001	50.300	92.748
	Un-controlled diabetic group	−181.50	6.811	<0.001	−197.548	−165.460
Uncontrolled diabetic group	Control group	253.03	9.010	<0.001	231.804	274.252
	Controlled diabetic group	181.50	6.811	<0.001	165.460	197.548

Statistical analysis: Tukey's HSD test. Statistically significant if $P<0.05$. HSD: Honest significant difference, SE: Standard error, CI: Confidence interval

Table 2a: Descriptive statistics for salivary glucose values

Salivary glucose value	Mean	SD	SE	95% CI for mean		Minimum	Maximum
				Lower bound	Upper bound		
Control group	1.20	0.27	0.04	1.13	1.28	0.70	1.70
Controlled diabetic group	2.48	0.81	0.07	2.34	2.62	1.10	3.90
Un-controlled diabetic group	3.37	0.81	0.07	3.23	3.52	2.00	4.90
Total	2.64	1.07	0.06	2.52	2.76	0.70	4.90

CI: Confidence interval, SD: Standard deviation, SE: Standard error

be statistically significant ($P = 0.019$) [Table 3a]. In the controlled diabetic group, the sera glucose levels ranged from 132 to 210 mg/dl with a mean of 171.1 mg/dl and a SD of 20.93 [Table 1a] against salivary glucose levels that ranged from 1.1 to 3.9 mg/dl with a mean of 2.48 mg/dl and a SD of 0.81 [Table 2a]. The correlation coefficient between sera and salivary glucose levels, in this group, gave an $R = 0.470$ which was again found to be statistically significant ($P = 0.031$) [Table 3b]. In the uncontrolled diabetic group, the sera glucose levels ranged from 213 to 490 mg/dl with a mean of 352.6 mg/dl and with a SD of 80.39 [Table 1a], whereas the salivary glucose levels ranged from 2 to 4.9 mg/dl with a mean of 3.37 mg/dl and a SD of 0.81 [Table 2a]. The correlation coefficient between sera and salivary glucose levels gave an $R = 0.498$ which was again statistically significant ($P = 0.039$) [Table 3c]. The difference in mean fasting sera glucose levels between the three groups was calculated using ANOVA one-way test and was found to be statistically significant ($P < 0.001$) [Table 1b]. The comparison between different groups using Tukey's HSD test revealed the difference in mean fasting sera glucose levels to be statistically significant between the control and the controlled diabetic groups ($P < 0.001$), control and uncontrolled diabetic groups ($P < 0.001$), and the controlled and uncontrolled diabetic groups ($P < 0.001$) [Table 1c]. The differences in the mean salivary glucose levels between the three groups were calculated by ANOVA one-way test and were also found to be statistically significant ($P < 0.001$) [Table 2b]. The comparison between different groups using Tukey's HSD test revealed the difference in mean fasting salivary glucose levels to be statistically significant between the control and controlled diabetic groups ($P < 0.001$), control and the uncontrolled diabetic groups ($P < 0.001$), and controlled and the uncontrolled diabetic groups ($P < 0.001$) [Table 2c]. Furthermore, there was a positive correlation between fasting sera and salivary glucose levels found with the *R* - value being 0.517 and *P* value being 0.019 in the control group [Table 3a], 0.470 and 0.031, respectively, in the controlled diabetic group [Table 3b] and 0.498 and 0.039, respectively, in the uncontrolled diabetic group [Table 3c].

Table 2b: Mean comparisons between groups using ANOVA one-way test

Source of variation	Sum of squares	df	Mean square	*F*	*P*
Between groups	173.461	2	86.731	155.163	<0.001 (significant)
Within groups	166.013	297	0.559		
Total	339.474	299			

Statistical analysis: ANOVA one-way test. Statistically significant if $P<0.05$

DISCUSSION

DM is a group of complex metabolic disorders that share the common underlying feature of hyperglycemia which results either from defects in insulin secretion or action, or most commonly, a combination of both. Currently, the diagnosis as well as regular monitoring of DM is achieved only by analyzing sera glucose levels (random, fasting, and/or postprandial), which is an invasive procedure. Furthermore, DM is a condition that requires a frequent monitoring of sera glucose levels in the body. This requirement of multiple pricking at regular intervals for monitoring sera glucose levels is physically and psychologically traumatic to most of the patients. Therefore, a noninvasive, simple, and painless procedure, such as salivary glucose estimation, is highly desirable to improve patient's compliance. This study was conducted with an aim to

Table 2c: Multiple comparisons between groups using Tukey's honest significant difference test

Group (I)	Group (J)	Mean difference (I–J)	SE	*P*	95% CI for mean	
					Lower bound	Upper bound
Control group	Controlled diabetic group	−1.28	0.125	<0.001	−1.570	−0.981
	Uncontrolled diabetic group	−2.17	0.125	<0.001	−2.464	−1.874
Controlled diabetic group	Control group	1.28	0.125	<0.001	0.981	1.570
	Uncontrolled diabetic group	−0.89	0.095	<0.001	−1.116	−0.671
Un-controlled diabetic group	Control group	2.17	0.125	<0.001	1.874	2.464
	Controlled diabetic group	0.89	0.095	<0.001	0.671	1.116

Statistical analysis: Tukey's HSD test. Statistically significant if $P<0.05$. HSD: Honest significant difference, SE: Standard error, CI: Confidence interval

Table 3a: Correlation analysis between serum and salivary glucose values in control group using Karl Pearson's correlation coefficient test

	Serum glucose value	Salivary glucose value
Serum glucose value		
Karl Pearson's correlation coefficient value (*r*)	1.000	0.517
P		0.019
Salivary glucose value		
Karl Pearson's correlation coefficient value (*r*)	0.517	1.000
P		0.019

Table 3b: Correlation analysis between serum and salivary glucose values in controlled diabetic group using Karl Pearson's correlation coefficient test

	Serum glucose value	Salivary glucose value
Serum glucose value		
Karl Pearson's correlation coefficient value (*r*)	1.000	0.470
P		0.031
Salivary glucose value		
Karl Pearson's correlation coefficient value (*r*)	0.470	1.000
P		0.031

Table 3c: Correlation analysis between serum and salivary glucose values in uncontrolled diabetic group using Karl Pearson's correlation coefficient test

	Serum glucose value	Salivary glucose value
Serum glucose value		
Karl Pearson's correlation coefficient value (*r*)	1.000	0.498
P		0.039
Salivary glucose value		
Karl Pearson's correlation coefficient value (*r*)	0.498	1.000
P		0.039

ascertain if a correlation exists between sera and salivary glucose levels. For this study, subjects were divided into three groups based on their fasting sera glucose levels. The criterion of fasting sera glucose levels was taken after studying the inferences from the study conducted by Rohlfing *et al*.[5] according to which patients with glycated hemoglobin (HbA1c) levels of >8% were supposed to have their sera glucose levels >205 and as per the recommendations of the American Diabetic Association (ADA),[6] HbA1c levels of >8% is indicative of a poor glycemic control although the advantages of using HbA1c test compared with the fasting sera glucose levels including greater convenience (fasting not required), greater preanalytical stability, and less day-to-day perturbations during stress and illness were masked by the lower sensitivity of HbA1c at the designated cut-point, higher cost, limited availability of HbA1c testing in certain regions of the developing world, and the imperfect correlation between HbA1c and average glucose in certain individuals. National Health and Nutrition Examination Survey data indicate that an HbA1c cut-point of >6.5% (48 mmol/mol) identifies one-third fewer cases of undiagnosed diabetes than a fasting glucose cut-point of >126 mg/dL (7.0 mmol/L). Furthermore, it is important to take age, race/ethnicity, and anemia/hemoglobinopathies into consideration when using the HbA1c to diagnose diabetes. Based on the above findings, this study considered fasting sera glucose levels as the criteria for categorizing the patients instead of HbA1c levels. From the results of the present study, it was found that the salivary glucose levels increased with sera glucose levels with the correlation coefficient between sera and unstimulated salivary glucose levels in the control subjects being 0.517, in controlled diabetics being 0.470 and in uncontrolled diabetics being 0.498 ($P < 0.05$). Forbat *et al*. conducted a study which revealed that salivary glucose concentration was independent of sera glucose levels. Although they used similar method (glucose oxidase) to estimate salivary glucose levels, the negative results could be attributed to the fact that they had used pure samples of parotid fluid rather than whole saliva as in most of the other studies.[7] Borg and Birkhed conducted a study to follow the secretion of free glucose in parotid saliva in various subjects after a single oral intake of different carbohydrates and compared the salivary glucose concentration with concentration in the sera. Salivary glucose concentration was analyzed enzymatically. The results of this study revealed that most of the 0^{th} min samples showed a variation in glucose concentration from 3 to 25 mmol/l. Furthermore, after glucose, fructose, and

sucrose intakes, the salivary glucose levels increased to about 2–4 times, especially in the 30th min samples. The correlation between the glucose concentration in saliva and sera was found to be higher after, then, before the carbohydrate intake.[8] Darwazeh *et al*. conducted a study, wherein salivary glucose levels were analyzed by modified enzymatic ultraviolet detection method and found glucose concentration in saliva of diabetics to be significantly higher than in the controls and directly related to the sera glucose levels.[9] Belazi *et al*. conducted a study to examine the flow rate and composition of unstimulated whole saliva and serum in children with newly diagnosed insulin-dependent DM (IDDM) and compared the values derived with the values obtained for a group of healthy controls although they observed no significant difference in the salivary flow rates between the two groups while significantly higher concentrations of glucose in the saliva and serum in children with IDDM. Salivary IgA concentration was also found to be higher in the test group as was serum IgG.[10] Amer *et al*. suggested that salivary samples of the nondiabetic control subjects did not show the presence of glucose even in the slightest concentrations while the samples obtained from the type 2 diabetics (non IDDM) showed significant concentration of glucose in the saliva.[11] López *et al*. demonstrated that total sugars, glucose, urea, and total proteins were greater in the diabetic patients than in the controls while calcium values were found to be decreased.[12] Aydin observed significantly higher salivary glucose levels in the diabetic patients when compared to the controls. Aydin, however, could not get any significant inter-group differences based on age and duration of the disease process.[13] Jurysta *et al*. conducted a study to evaluate salivary glucose concentration in unstimulated and mechanically stimulated salivary samples in the normal, healthy controls and diabetic patients and observed higher glucose concentration in the saliva of diabetic patients than in the controls. Sera glucose levels were measured by glucose oxidase method while salivary glucose levels were assessed by hexokinase method in their study. Furthermore, they found no significant difference between unstimulated and stimulated salivary samples when compared with the sera glucose levels in the diabetic patients. Only unstimulated salivary samples were, therefore, considered for analysis in the present study.[14] Soares *et al*. concluded from their study that the concentration of salivary glucose was not dependent on capillary glycemia. The levels of salivary glucose also seemed to be unaffected by variables including gender of the patients.[15] Panchbhai *et al*. observed significantly elevated mean salivary glucose levels in both uncontrolled and controlled diabetic patients when compared with the healthy controls in accordance with the results of the present study.[16] Sashikumar and Kannan conducted a study to assess salivary glucose concentration and oral candidal carriage in type 2 diabetic subjects and found higher salivary glucose levels in the diabetics than in the nondiabetic subjects similar to the findings of the present study. Diabetic status was determined by assessment of random, nonfasting sera glucose levels, and glycosylated hemoglobin (HbA1c) levels. Salivary glucose levels were measured in the unstimulated and stimulated salivary samples by glucose oxidase method. Furthermore, a significant positive correlation was observed between salivary and sera glucose levels in addition to the finding that increased salivary glucose was also associated with increased the prevalence of oral candida in such patients.[17] Vasconcelos *et al*. conducted a study to evaluate the correlation between sera and salivary glucose levels, wherein the saliva was stored frozen until use in the glucose assay while the absorbance values of salivary glucose assay were read on a spectrophotometer at wavelength of 500 nm. Salivary glucose concentration was found to be significantly higher in type 2 diabetics although they could not observe a significant positive correlation between salivary and sera glucose levels in diabetic patients which was in contrast to the results of the present study. Furthermore, they suggested that since salivary glucose levels are not directly influenced by glycemia, salivary assessment of glucose cannot be used to monitor glycemic control in diabetics.[18] Bakianian Vaziri *et al*. observed no significant difference in the glucose concentrations between type 1 and type 2 diabetic patients and their matched controls contradictory to the results of the present study, wherein a strong positive correlation was seen. They concluded that since alterations in the oral cavity might have some role in the development and severity of oral changes, determination and monitoring of salivary constituents might be useful in the management of oral findings in diabetic patients.[19] Nagalaxmi and Priyanka obtained a significant correlation between salivary and sera glucose levels in type 1 diabetic patients and in the controls. The levels of salivary glucose, also, seemed to be unaffected by variables including age and gender of the patients.[20] Lasisi and Fasanmade conducted a study to determine the effects of type 2 DM and periodontal disease on salivary flow rates and biochemical composition including salivary glucose and potassium levels and found significantly higher values in the diabetic patients regardless of the periodontal disease status compared with the nondiabetic subjects in accordance with the findings of the present study.[21] Abikshyeet *et al*. conducted a study to substantiate the role of saliva as a diagnostic tool in the monitoring of DM. The results of the study revealed increased fasting salivary glucose levels in patients with DM with a significant positive

correlation observed between salivary and sera glucose levels in the diabetic as well as controls. Based on their results, they concluded that fasting salivary glucose levels can be used as a noninvasive diagnostic and monitoring tool to assess the glycemic status in diabetic patients.[22] Panchbhai conducted a study wherein a significant positive correlation was observed between salivary and fasting sera glucose levels in subjects with uncontrolled DM.[23] Agrawal *et al*. in their study found the correlation coefficients for nondiabetic and diabetic patients to be +0.58 and +0.40, respectively, proving the correlation between fasting salivary and sera glucose levels statistically significant in accordance with the results of the present study. They grouped diabetic and nondiabetic patients based on age although the levels of salivary and sera glucose levels were found to be unaffected by the variable as was observed in the previous studies.[24] Prathibha *et al*. also stated that significant variations were observed in salivary physical and biochemical parameters between the diabetic and nondiabetic subjects.[25] The results of the present study were, also, in accordance with the findings of a recent study conducted by Jha *et al*. who concluded that salivary glucose levels were significantly higher in the diabetic than in the nondiabetic patients. Furthermore, they observed a significant positive correlation between salivary and sera glucose levels. The diabetic status in the subjects, in their study, was determined by the estimation of random, nonfasting sera glucose levels and glycosylated hemoglobin (HbA1c) levels.[26] Thus, on reviewing the literature so far, it could be inferred that saliva can be used as a potentially useful, noninvasive tool in the regular monitoring of diabetic patients. Numerous studies have shown a significant positive correlation between salivary and sera glucose levels, however, the specificity of the salivary glucose assay to assess the exact sera glucose levels still remains a big question. There is a controversy regarding the relationship between the concentration of glucose in the sera and the salivary fluid. Several factors might account for the poor correlation between sera and salivary glucose levels prevailing in diabetic patients including oral retention of alimentary carbohydrates, glucose utilization by bacteria, release of carbohydrates from salivary glycoproteins, and contamination of the saliva by a large outflow of gingival crevicular fluid in patients with poor gingival status. Abikshyeet *et al*. formulated equations to predict fasting sera glucose levels and HbA1c percentage when fasting salivary glucose levels were known, however, accurate sera glucose levels could not be assessed by such equations in all the subjects.[22]

Controversy and future research directions

Thus, on reviewing the literature so far, it could be inferred that saliva can be used as a potentially useful, noninvasive tool in the regular monitoring of diabetic patients. Numerous studies have shown a significant positive correlation between salivary and sera glucose levels, however, the specificity of the salivary glucose assay to assess the exact sera glucose levels still remain a big question. There is a controversy regarding the relationship between the concentration of glucose in the sera and the salivary fluid. Several factors might account for the poor correlation between sera and salivary glucose levels prevailing in diabetic subjects including oral retention of alimentary carbohydrates, glucose utilization by bacteria, and release of carbohydrates from salivary glycoproteins and contamination of the saliva by a large outflow of gingival crevicular fluid in patients with poor gingival status. Abikshyeet *et al*. formulated equations to predict fasting sera glucose levels and HbA1c percentage when fasting salivary glucose levels were known. However, accurate sera glucose levels could not be assessed by such equations in all the subjects.[22] Based on the presently available data, there is an obvious need for further, extensive studies, to obtain an answer to this query, to accurately assess sera glucose levels from the obtained salivary glucose levels and utilizing the diagnostic benefits of saliva in the clinical practice for the exact estimation of sera glucose levels.

Limitations of the model for using saliva in diagnostics

Apart from the above mentioned limitations, the potential use of saliva in diagnosis as well as in the regular monitoring of diabetic patients suffers from another possible constraint wherein in certain situations including numerous auto-immune and/or inflammatory conditions such as Sjogren's syndrome and primary biliary cirrhosis, graft versus host disease, IG-G4-related sclerosing disease, degenerative diseases such as amyloidosis, granulomatous conditions including sarcoidosis, infections including HIV/AIDS, hepatitis C, malignant conditions such as lymphomas and salivary gland agenesis or aplasia apart from drug-induced xerostomia caused due to drugs including anticholinergics, antihistamine , antihypertensives, and neurotropic drugs including sedatives and anxiolytics, anti-depressants and anti-psychotics, to name a few, either a decreased salivary output/xerostomia or a possible change in salivary composition is seen and the total solids in the saliva change to the extent of not being reliable for diagnostics as well as in the regular monitoring of the patients. Patients with salivary gland changes after exposure to radiation in the head and neck area for treatment of malignancies also pose such challenges. Similar challenges are faced even in situations wherein the glucose threshold is either exceeded as in hyperglycemic crisis like diabetic ketoacidosis due to xerostomia or in cases of severe hypoglycemia because serum glucose levels have to cross a minimum threshold to appear in saliva.

CONCLUSION

On the basis of the results of the study, it could be concluded that saliva contains glucose which varied in proportions with serum glucose levels and this correlation between salivary and sera glucose levels was found to be significant. Thus, saliva offers an alternative to serum that can be analyzed for the diagnosis and regular monitoring of the control of disease process in DM patients. Seeing the present prevalence of DM on such a large scale globally, the analysis of saliva can offer a reliable, noninvasive and cost-effective approach for the screening of large populations, thereby, preventing the morbidity and mortality associated with this dreadful and complex metabolic disorder which seems to be attacking people in all age groups, genders and with varied socioeconomic status.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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