Original Research

Study Of Correlation Between Salivary And Serum Glucose Levels In Diabetic And Non Diabetic Individuals

[1]Dr Sarib Gul, [2]Dr Samreen Gul, [3]Dr Saqib Gul

[1]MDS, Ex-Resident, Department of Oral and Maxillofacial Radiology, Vyas Dental College and Hospital, Rajasthan.
[2]MS, Resident, Department of ENT&HNS, Government Medical College Srinagar.
[3]MD, Senior Resident, Department of Physiology, Government Medical College, Udhampur

Corresponding Author
Dr. Saqib Gul
MD, Senior Resident, Department of Physiology, Government Medical College, Udhampur

Received: 29 November, 2023 Accepted: 10 December, 2023

Abstract
Aim: To study correlation between salivary and serum glucose levels in diabetic and non diabetic individuals.
Materials And Methods: The present cross sectional study was conducted among 100 patients of confirmed diagnosed cases of type I and type II diabetes mellitus visiting the Department Of Oral Medicine and Radiology, Vyas Dental College and Hospital and the General Hospital of Vyas Dental College, Jodhpur. The fasting blood glucose levels and the unstimulated salivary samples were collected in study and control groups.
Results: Salivary glucose level was found to be significantly more among subjects suffering from diabetics (18.43±4.30 mg/dl) than non diabetics (7.09±2.37 mg/dl). Similarly, Serum glucose level was found to be significantly more among subjects suffering from diabetics (170.89±61.36 mg/dl) than non diabetics (107.10±16.28 mg/dl). There was strong positive correlation between serum and salivary glucose in case and control group.
Conclusion: Our result emphatically shows the positive statistical co-relation between the salivary glucose and the serum glucose thus, assessment of the salivary glucose can be established as a non-invasive tool for diagnosis and monitoring the diabetes mellitus. Thus it can be inferred that saliva can be used as an alternative to blood for diagnosing and monitoring diabetes mellitus status as it is noninvasive compared to other fluids and can be easily used in children, elderly, critically ill and debilitated patients.
Keywords: Diabetes, Saliva, Glucose

Introduction: Diabetes mellitus is a complex multi systemic metabolic disorder characterized by a relative or absolute deficiency of insulin secretion and/or concomitant resistance to the metabolic action of insulin on target tissues. The prevalence of DM for all age groups worldwide was estimated to be 2.8% in 2000 and may reach 4.4% by 2030. Additionally the diabetic population is expected to rise from 171 million in 2000 to 366 million by 2030. Recent World Health Organization calculations indicated that worldwide almost 3 million deaths per year are attributed to diabetes, equivalent to 5.2% of all deaths.[1]It is characterized by symptoms of excessive thirst (polydipsia), excessive hunger (polyphagia), excessive passing of urine (polyurea). These symptoms are also termed as 'osmotic symptoms'. These symptoms are attributed to presence of high glucose levels in blood. Diabetes is often diagnosed by a simple blood test taken either after fasting (70-110mg/dl) overnight or a random sample (70-140mg/dl) at any time or by doing HbA1C levels (3.5-5.7%) in blood. Urine examination may assist in diagnosis by showing presence of glucose or Ketone bodies, if the blood sugar goes above 180 mg/dl (renal threshold). Since the diagnosis involves withdrawing of blood samples frequently, it becomes a painful procedure and patients usually don't cooperate. Glucometers are currently used which do not utilize blood samples used for routine blood investigations but a pin prick may give accurate blood sugar levels and can be performed at home with ease.[2-4] Researches are being conducted to devise new diagnostic and therapeutic methods for analyzing glucose levels in the blood. One of the methods is estimating glucose levels in saliva, which if proved conclusive can be a good tool in the hands of doctors to treat the diabetic patients.[4]The current study is comparative in nature and involves both blood testing and salivary testing for determination of glucose concentrations. Glycosylated hemoglobin shows the degree of glycemic control during the preceding three months. Since blood testing is invasive in nature and

involves discomfort to the patient, so various methods have been tested to diagnose and monitor diabetes mellitus. The purpose of the current study is to find out if there exists any correlation between salivary and serum glucose levels in diabetic and non diabetic individuals.

Materials And Methods: The present cross sectional study was conducted among 100 patients of confirmed diagnosed cases of type I and type II diabetes mellitus visiting the Department Of Oral Medicine and Radiology, Vyas Dental College and Hospital and the General Hospital of Vyas Dental College, Jodhpur.

Inclusion criteria: Patients with age>40 years having confirmed diagnosed cases of type I and type II diabetes mellitus.

Control group: 100 patients without any history of diabetes mellitus and other systemic diseases, not taking any systemic drug therapy and whose serum glucose levels are within normal limits.

Exclusion criteria:

1. Patients with history of salivary gland disorders.
2. Patients receiving radiotherapy or long drug therapy for other diseases.
3. Patients with history of systemic diseases, endocrinal or metabolite in nature which can affect serum plasma levels.

Method: The fasting blood glucose levels and the unstimulated salivary samples were collected in study and control groups. The fasting assessment of saliva was carried out before any other dental procedure. Salivary sample collection was performed in the morning between 9.00–11.00 am to avoid circadian variations. The patients were asked to rinse their mouth with distilled water and asked to relax for 5 minutes. The patients were asked to lean their head forward over the test tube and open their mouth slightly and saliva was allowed to drain into the tube for about 5 minutes. Any remaining saliva after 5 minutes was spit into the test tube. One millilitre of each unstimulated saliva sample was centrifuged at 3000rpm for 20 minutes and clear supernatants were processed immediately for estimation of glucose. Supernatants were stored at -70^{0}C for further analysis. Glucose levels of unstimulated saliva was stimated using Glucose oxidase kit (Autospan cogent and Abcam) in semi automated analyzer. 1000µl of reagent was mixed with 10µl of salivary sample and incubated at 37^{0}C for 10 mins. The absorbant values of the sample and standard was measured at 505 nm by semi automatic analyzer. Values were analyzed as milligrams/deciliters (mg/dl).

Statistical analysis: The statistical software namely SPSS 26.0 was used for the analysis of the data to generate graphs, tables etc. Chi square and Fisher exact test have been used to test the significance of proportions of stimulated saliva and unstimulated saliva between cases and controls. Student T test has been used to find the significance of unstimulated saliva and stimulated saliva between cases and controls. Analysis of variance has been used to find the significance of trend with CFU/ml. Chi square test and Fisher exact test have been used to test the significance of proportions CFU/ml between cases and controls. Pearson correlation was used to find relation between C.CFU with unstimulated saliva.

Results: It was showed that there were total of 100 subjects who were diabetics and were recruited in the present study. Among those 100 subjects, 64% were in the age category of 41-60 years. Gender wise distribution showed that there were total of 46 males and 54 females in Case group where as there were 57 males and 43 females among controls. Around 58 % of the study population was suffering from diabetes for more than 6 years.

Table 1: Age wise distribution of the study population

Groups		Age Group				Total
		≤40 years	41-50 years	51-60 yeas	>60 years	
Group I- Cases (Diabetics)	N	19	32	32	17	100
	%	19.0%	32.0%	32.0%	17.0%	100.0%
Group II- control (Non diabetics)	N	24	35	28	13	100
	%	24.0%	35.0%	28.0%	13.0%	100.0%
Total	N	43	67	60	30	200
	%	21.5%	33.5%	30.0%	15.0%	100.0%
P value	0.679 (NS)					

Chi square test, significance level at p<0.05, NS: non-significant

Table 2: Gender wise Distribution of study population

Groups	Males	Females	Total
Group I- Cases (Diabetics)	46	54	100
Group II- control (Non diabetics)	57	43	100
Total	103	97	

Table 3: Comparison of Salivary glucose level among study groups

Groups	Mean Salivary Glucose level	SD
Group I- Cases (Diabetics)	18.4315	4.30874
Group II- control (Non diabetics)	7.0919	2.37452
P value	<0.0001*	

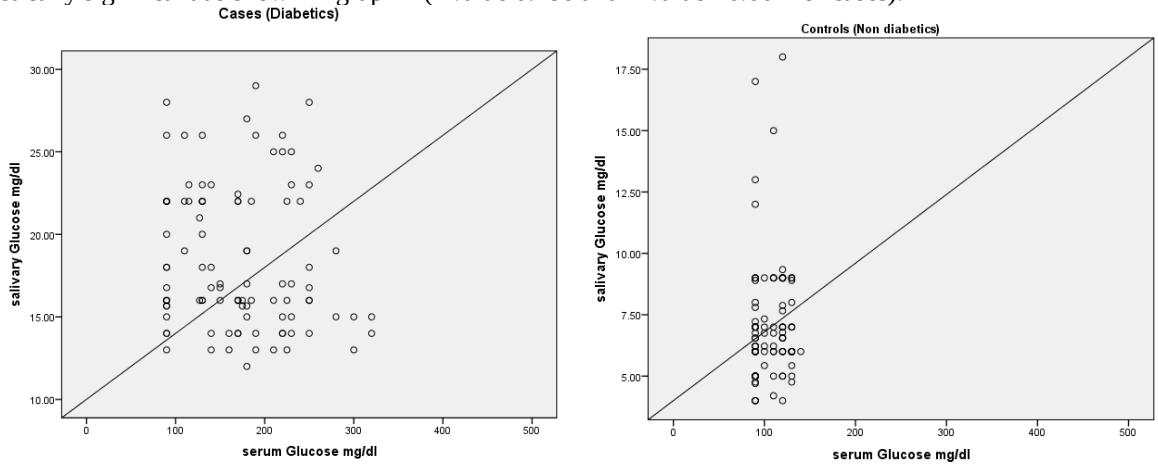
Independent t test, significance level at p<0.05

Table 4: Comparison of Serum glucose level among study groups

Groups	Mean Serum Glucose level	SD
Group I- Cases (Diabetics)	170.89	61.369
Group II- control (Non diabetics)	107.10	16.286
P value	<0.0001*	

Independent t test, significance level at p<0.05

There was strong positive correlation between serum and salivary glucose in case and control group which was statistically significant as shown in graph 1 (r-value 0.786 and P value <0.001 for cases).



Graph 1: Correlation between serum and salivary glucose in case and control

Discussion: Saliva is the easiest sample that can be collected noninvasively with minimal armamentarium and is associated with fewer compliance problems as compared to blood. Therefore the non invasive technique of glucose estimation by the use of saliva can be the most valuable substitute for previously establish different invasive test. Chronic hyperglycemia may lead to metabolic disregulation and failure of various organs, especially eyes, kidneys, nerves, heart, and blood vessels. However, blood collection is an invasive procedure and is more costly as it requires the help of a trained technician and the use of sharps.[1] Type 2 diabetes may remain undetected for years. The simple procedure may enable even the healthy subjects to approach the diabetic clinic for routine check-up, thus the apparently healthy patients can get diagnosed for diabetes mellitus as earlier they get diagnosed, lesser will be the complications. Glucose, a small molecule can easily diffuse through semi permeable membranes thus increasing the salivary glucose levels, which ultimately results in consequent loss of homeostasis and greater susceptibility to diseases in the oral cavity. Normal glucose levels in saliva are 0.5–1.00 mg/100 ml and do not considerably have an effect on oral health or support the growth of microorganisms. Thus the present study was initiated with the aim to assess the correlation between salivary and serum glucose levels in diabetes mellitus and non diabetic individuals and to devise non invasive methods for management of diabetes. Salivary glucose level was found to be significantly more among subjects suffering from diabetics (18.43±4.30 mg/dl) than non diabetics (7.09±2.37 mg/dl). Similarly, Serum glucose level was found to be significantly more among subjects suffering from diabetics (170.89±61.36 mg/dl) than non diabetics (107.10±16.28 mg/dl). The result of the study confirmed that salivary glucose is higher in diabetic group when compared with healthy individuals, which is in accordance to the study done by Agrawal et al[5] and Amer et al.[6] It is possibly due to the increase permeability of the basement membrane and leakage of the microvasculature in the diabetes mellitus, which allows the easy access for the glucose in the saliva. The complications of the diabetes results due to the micro-vascular changes in blood vessels and change in the basement membrane in diabetic patients. Many theories have been put forth to explain the micro-vascular alterations. Hyperglycemia leads to increased advance glycosylation end products, commonly known as ―AGEs. These AGEs crosslink proteins such as collagen and extracellular matrix proteins, leading to alteration of basement membrane which in turn results to endothelial dysfunction. This alters the microvasculature structure and makes it more permeable. Other products such as sorbitol, diacyl glycerol, and fructose 6-phosphate, which are formed because of the chronic hyperglycemia, also

lead to the basement membrane alterations by altering the extracellular matrix proteins. The end result is the leaky basement membrane, which explains the increase passage of glucose from the blood into the saliva in diabetes mellitus.[7] Strong positive correlation between serum and salivary glucose which was statistically significant as well for cases as well as controls was also observed in the present study. Hence, salivary glucose appears to be an indicator of serum glucose concentration in diabetic patients. Similar to our study, Reuterving et al[8] too found a positive correlation between salivary glucose and serum glucose.

Salivary glucose concentration was found directly proportional to serum glucose concentration. These findings were consistent with the findings by Sreedevi et al[9], Englander et al[10], Thorstensson et al[11], Agrawal et al[5] and Akasapu et al[12] who all reported increase in salivary glucose level in patients of diabetes mellitus in comparison to non diabetics. Conversely lack of the correlation between salivary glucose and plasma glucose was observed by Marchetti et al[13] in fasting state in both diabetic and non diabetic and that indicates the degree of the metabolic control does not effects the way of the salivary gland handle the glucose. Also the study by Forbat et al[14] shows no significant correlation between the salivary and plasma glucose. In those studies old method of the glucose estimation were used, which was not appropriate. Also the researcher England et al expressed doubt regarding replacement of the serum as the sample with parotid secretion in the diagnosis of diabetic mellitus because of the lower level of the glucose concentration in the saliva as compared to the serum. Some of the studies have contradicted the correlation between Salivary Glucose level (SGL) and Blood glucose level (BGL). It was suggested that saliva cannot be implemented to indicate BGL in diabetics as the amount of damage to the salivary gland in turn the quantity of leakage of glucose from plasma to saliva is unpredictable. Twetman et al[15] justified the threshold mechanisms along the basement membrane; hence rejected the possibility of existence of any relationship between serum and saliva glucose. India has distinction of being the country having higher prevalence of diabetes mellitus; the present study is of great concern in context to Indian population as well as globally to the countries with the greater prevalence of diabetes. The present study highlights the importance of early diagnosis and the utilization of non-invasive saliva analysis over the invasive blood analysis. To our knowledge, present research is one of those few studies that have included the evaluation of the critical correlation of SGL and BGL

Limitations: The study has unquestionably put forth some observations deserving explanation, which likely suggests enormous scope for further research though the study results were inconclusive due to relatively insufficient sample size.

Conclusion: Our result emphatically shows the positive statistical co-relation between the salivary glucose and the serum glucose thus, assessment of the salivary glucose can be established as a non-invasive tool for diagnosis and monitoring the diabetes mellitus. Thus it can be inferred that saliva can be used as an alternative to blood for diagnosing and monitoring diabetes mellitus status as it is noninvasive compared to other fluids and can be easily used in children, elderly, critically ill and debilitated patients. Oral diagnosticians are advised to screen the diabetic patients for any oral infections at the earliest and further institute the management for the same. However, further studies need to be undertaken involving larger sample size, using different methods of saliva and blood collection, by taking glycosylated hemoglobin to estimate blood glucose levels. The standardized procedure of salivary glucose estimation for Diabetes Mellitus may herald a new era in non invasive method of diagnosis.

References

1. Manfredi M, McCullough MJ, Vescovi P, Al-Kaarawi ZM, Porter SR. Update on diabetes Mellitus and related oral diseases. Oral Dis 2004;10:187-200.
2. Malamed Stanley F.Medical emergencies in the dental office. 6th ed Missouri: Mosby;2000.
3. Forbat LN, Collins RE, Maskall GK, Sonksen PH. Glucose Concentrations in Parotid Fluid and venous blood of patients attending a diabetic clinic. J Royal Soc Med 1981;74:725-8.
4. Kumar S, Padmashree S, Jaya Lekshmi R. Co-relation of salivary glucose, blood glucose and oral candidal carriage in the saliva of type 2 diabetics: A case control study. Contemp Clin Dent 2014;5:312-7.
5. Agrawal RP, Sharma N, Rathore MS, Gupta VB, Jain S, Agarwal V, et al. Noninvasive Method for Glucose Level Estimation by Saliva. J Diabetes Metab 2013;4:266.
6. Amer S, Yousuf M, Siddiqui PQ, Alam J. Salivary glucose concentrations in patients with diabetes mellitus: A minimally invasive technique for monitoring blood glucose levels. Pak J Pharma Sci 2001;1433-7.
7. Reinauer H, Home PD, Kanagasabapathy AS, Heuck CC. Laboratory Diagnosis and Monitoring of Diabetes Mellitus. Geneva: WHO; 2002.
8. Reuterving CO, Reuterving G, Hägg E, Ericson T. Salivary flow rate and salivary glucose concentration in patients with diabetes mellitus influence of severity of diabetes. Diabete Metab 1987;13(4):457-462.
9. Sreedevi, Shashikanth MC, Shambulingappa P. Com- parison of serum glucose and salivary glucose in diabetic patients. J Indian Acad Oral Med Radiol 2008;20(1): 9-13.
10. Englander HR, Jeffay AI, Fuller JB, Chauncey HH. Glucose concentrations in blood plasma and parotid saliva of individuals with or without diabetes mellitus. J Dent Res 1963;42:1246.
11. Thorstensson H, Falk H, Hugoson A, Olsson J. Some salivary factors in insulin-dependent diabetics. Acta Odontol Scand 1989;47(3):175-183.
12. Akasapu A, Hegde U, Nitin P. Correlation of Blood Glucose Levels with Salivary Glucose Levels in Type 2 Diabetes Mellitus: A Comparative Study. Current Trends in Biomedical Engineering and Biosciences.

2017;6: 1-4.
13. Marchetti P, Tognarelli M, Giannarelli R, Grossi C, Picaro L, di Carlo A, Benzi L, Ciccarone A, Navalesi R. Decreased salivary glucose secretory rate: usefulness for detection of diabetic patients with autonomic neuropathy. Diabetes Res Clin Pract. 1989;7(3):181-6.
14. Forbat LN, Collins RE, Maskell GK, Sönksen PH. Glucose concentrations in parotid fluid and venous blood of patients attending a diabetic clinic. J R Soc Med. 1981;74(10):725-8.
15. Twetman S, Nederfors T, Stahl B, Aronson S. Two-year longitudinal observations of salivary status and dental caries in children with insulin-dependent diabetes mellitus. Pediatr Dent. 1992;14(3):184-8.