

Evaluation of Salivary Glucose and Creatinine for Screening of Diabetes and Kidney Disease

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Abstract

Objective: Diabetes mellitus is a multifactorial metabolic disorder that affects multiple organs of the body, one of the most important of which is chronic kidney disease. Early diagnosis of this disease is suggested as an important strategy to reduce the complications of the disease worldwide. Since the measurement of salivary creatinine and glucose is an easy and noninvasive method, the aim of this study was to evaluate the serum and salivary levels of creatinine and glucose for screening of diabetes and kidney disease.

Materials and Methods: This cross-sectional study was performed on 50 seemingly healthy individuals referred to the Department of Oral Medicine of the Faculty of Dentistry. Serum and salivary creatinine levels were measured in these individuals. Data (mean \pm standard deviation) were presented for variables. Data were analyzed by SPSS 19 software. Pearson correlation coefficient was used to determine the correlation between serum and salivary levels of creatinine and glucose. *P*-values less than 0.05 were considered significant.

Results: The mean salivary and serum creatinine levels was reported to be 0.27 (\pm 0.29) and 0.90 (\pm 0.12) mg/dl, respectively. Also, the mean salivary and serum glucose levels were reported to be 3.1 (\pm 0.7) and 88.92 (\pm 6.16) mg/dl, respectively. The results of Pearson correlation test showed no significant correlation between serum and salivary glucose and creatinine.

Conclusion: The use of non-invasive diagnostic methods such as saliva is of great value. The study found no association between serum and salivary creatinine and glucose in seemingly healthy subjects.

Keywords: Saliva, Serum, Creatinine, Glucose

Introduction

Diabetes mellitus is a multifactorial metabolic disorder caused by a defect in insulin secretion or insulin resistance. Diabetes is considered a major public health problem in many parts of the

world and Iran. Early diagnosis of diabetes is suggested as an important strategy to reduce the complications of the disease worldwide. This metabolic disorder affects multiple organs of the body, one of the most important

of which is chronic kidney disease (1). Chronic kidney disease is a progressive decline in kidney function. Kidney damage reduces the glomerular capacity of the kidneys and subsequently leads to elevated serum levels of metabolic byproducts (2,3).

Creatinine blood testing is the most common marker for the presence and progression of chronic kidney disease, so with worsening kidney disease and nephrons loss, serum creatinine levels will rise (4). Diagnosis of these diseases is now largely dependent on results from blood tests, urine tests, biopsies and physical examinations (5). Blood sampling is an invasive procedure that causes stress and discomfort to patients. Patients also lose about 4 to 20 ml of blood during each dialysis, which is exacerbated by multiple blood sampling (6).

In addition, dialysis patients are at increased risk for hepatitis B and C, which has a high chance of transmitting the infection to the laboratory staff when blood sampling is performed (7). Saliva is a biological fluid that is secreted by the salivary glands. Saliva collection is simple, noninvasive, and economical and is collected by the patient with the least intervention of medical staff. When it comes to repeat testing it is easily obtained and is suitable for all age groups. It is also a cost-effective method for screening large populations and is a good alternative to blood sampling in patients with coagulation problems such as hemophilia and patients with venous access problems (8).

Given that studies to date have examined the relationship between serum and salivary levels of glucose and creatinine in patients with diabetes and kidney disease, and this relationship has not been evaluated in apparently healthy individuals, our research hypothesis was: There is no association between serum levels and glucose and creatinine in apparently healthy individuals. Thus, the aim of this study was to evaluate the serum and salivary levels of creatinine and glucose in apparently healthy subjects in the Tabriz Dental School.

Materials and Methods

Sample size

Based on the article by Venkatesh et al., (10) which was related to this study, 50 individuals were assigned to this study, considering $\alpha=0.05$ and a power of 80%.

Subjects

This cross-sectional study was performed on 50 healthy individuals referred to the Department of Oral Medicine of Tabriz Faculty of Dentistry in 2018 who were randomly selected. Inclusion criteria included apparently healthy individuals between the ages of 30 and 50 years old who do not have a known disease and consent to participate in the study. Exclusion criteria included history of cardiovascular disorders (such as coronary artery diseases or hypertension), diabetes mellitus, malignant diseases, immunodeficiency, current pregnancy or lactation, smoking, taking corticosteroids in the last 6 months, BMI above 30 kg / m², and diseases of the thyroid and adrenal glands.

Sampling

After consent was completed, serum samples were prepared and un-stimulated saliva samples were collected concurrently with Navazesh technique (5). In such a way that participants should not eat or drink anything two hours before sampling. 15 minutes before sampling, the volunteers washed their mouths, and then their oral cavity was examined with adequate light and mirrors for assuring of no material in the oral cavity. The patient's saliva samples were collected within 16-20 minutes using sterile disposable plastic container and transferred to the laboratory immediately. In the laboratory the saliva samples were centrifuged at 10,000 rpm for 1 minute and the supernatant was poured into a micro-tube. Serum and salivary glucose and creatinine levels were analyzed using spectrophotometric assay. The HITACHI® 902 automatic analyzer was used.

Statistical analysis

Data (mean \pm standard deviation) were presented for variables. Pearson correlation coefficient was used to determine the correlation between serum and salivary levels of creatinine and glucose. Data were analyzed by SPSS 19 software. *P*-values less than 0.05 were considered significant.

Ethical considerations

Participants in this study were consented and no unnecessary intervention was performed. Therefore, this study had no adverse effects on patients and their therapeutic process. It should be noted that the approval of the Research Ethics Committee of Tabriz University of Medical Sciences has also been obtained by Code of Ethics (IR.TBZMED.REC.1398.163).

Results

In this study, 50 persons were included, of whom 20 (40%) were male and 30 (60%) were female. The mean age of participants was 32.4 (\pm 5.5) years.

The mean salivary and serum creatinine levels were reported to be 0.27 (\pm 0.29) and 0.90 (\pm 0.12) mg/dl, respectively. Also, the mean salivary and serum glucose levels were reported to be 3.1 (\pm 0.7) and 88.92 (\pm 6.16) mg/dl, respectively (Table 1).

The results of Pearson correlation test (Table 2) showed no significant correlation between serum and salivary creatinine and glucose (*P*-value= 0.675, *P*-value= 0.227). These results indicate that salivary levels of glucose and creatinine cannot be used to estimate their serum levels in apparently healthy individuals.

Discussion

The analysis of salivary compounds may be used as a non-invasive method in the diagnosis and screening of various systemic diseases, including chronic kidney disease and diabetes. Early screening and diagnosis of these diseases are important to preventing cardiovascular events and other complications. Creatinine is a by-product of metabolism that is excreted by the kidneys. All creatinine that enters the glomeruli is excreted without reabsorption, so its amount in the blood can be a marker of kidney function. Normal serum creatinine is 0.6-1.5 mg/dl and salivary value is 0.05-0.2 mg/dl (4), which is consistent with our results. In this study, it was concluded that in healthy subjects, there was no significant correlation between serum and salivary creatinine.

This result is in agreement with the results of a number of studies indicating the absence of this association in healthy subjects (10,11). In healthy subjects, creatinine is unable to diffuse through cells and tightly inter-cellular bind of salivary gland due to its high molecular weight and solubility in fat, but salivary creatinine levels increase in disease conditions may be due to changes in salivary cell permeability. It is found that elevated serum creatinine in renal patients produces a gradient concentration that facilitates the release of creatinine from serum to saliva (10).

Accordingly, it was shown that there was a statistically significant association between serum creatinine and saliva in chronic renal patients, whereas this association was not observed in healthy subjects (10,11). However, studies by Lasisi et al and Sedkey et

Table 1. Mean and standard deviation of serum and salivary creatinine and salivary glucose

Variable	Mean \pm Standard deviation (mg/dl)
Salivary creatinine	0.27 (\pm 0.29)
Serum creatinine	0.90 (\pm 0.12)
Salivary glucose	3.1 (\pm 0.70)
Serum glucose	88.92 (\pm 6.16)

Table 2. The results of correlation between serum and salivary creatinine and glucose

Variable pairs	The correlation coefficient of pearson test	<i>P</i> -value*
Serum creatinine & salivary creatinine	0.068	0.675
Serum glucose & salivary glucose	0.195	0.227

* Pearson test

al. showed that there was a significant positive correlation between serum creatinine and saliva concentrations in both healthy and chronic renal patients (12,13). The differences appear to be due to differences in sample numbers, inclusion criteria, different sample populations; different saliva sampling methods or different creatinine analysis methods.

Lack of association between salivary and serum glucose was another result of this study. Glucose is a small molecule that enters the saliva in patients with diabetes because of increased permeability of the cell membrane of marginal gingival cells. As blood glucose rises above the threshold, it also causes the release of glucose from the basement membrane of the salivary glands, especially the parotid gland, and increases the amount of salivary glucose while this mechanism is not present in healthy individuals. (14). Increased salivary glucose in diabetic patients due to elevated serum glucose can be explained in several ways. Increased blood glucose is associated with increased production of advanced glycosylation end products (AGEs) and other byproducts, leading to increased endothelial cells permeability through chemical bonding with extracellular matrix proteins and disruption of basement membrane (15). In a number of studies examining the relationship between serum and salivary

glucose levels, salivary glucose levels are only correlated with serum glucose levels in diabetic patients (16), but Gupta et al. (17) as well as Bhattacharyya et al. (18) have been reported in diabetic patients as well as in healthy subjects.

Limitation of the study is that composition of saliva changes in different conditions leading to alteration in salivary compound (19). Further studies suggested evaluating the diagnostic value of salivary glucose and creatinine levels in the early diagnosis of disease.

Conclusions

The use of non-invasive diagnostic methods such as saliva is of great value. The study found no association between serum and salivary creatinine and glucose in healthy subjects.

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Conflict of Interest

There are no conflicts of interest.

References

1. Nishimura A, Matsumura K, Kikuno S, Nagasawa K, Okubo M, Mori Y, et al. Slowly Progressive Type 1 Diabetes Mellitus: Current Knowledge And Future Perspectives. *Diabetes Metab Syndr Obes.* 2019;12:2461-77.
2. Gluck C, Qiu C, Han S, Palmer M, Park J, Ko Y, et al. Kidney cytosine methylation changes improve renal function decline estimation in patients with diabetic kidney disease. *Nat Commun.* 2019;10:2461.
3. Yu S, Joseph V. Bonventre Acute Kidney Injury and Progression of Diabetic Kidney Disease. *Adv Chronic Kidney Dis.* 2018;25(2):166-80.
4. Daugirdas J, Depner T. Creatinine generation from kinetic modeling with or without postdialysis serum creatinine measurement: results from the HEMO study. *Nephrol Dial Transplant.* 2017;32(11):1926-33.
5. Modhumi Khan R, Chua Z, Tan J, Yang Y, Liao Z, Zhao Y. From Pre-Diabetes to Diabetes: Diagnosis, Treatments and Translational Research. *Medicina (Kaunas).* 2019;55(9):546.
6. Sapiiano M, Savinkina A, Ellingson K, Haass K, Baker M, Henry R, et al. Supplemental Findings from the National Blood Collection and Utilization Surveys, 2013 and 2015. *Transfusion.* 2017;57(2):1599-624.
7. Garthwaite E, Reddy V, Douthwaite S, Lines S, Tyerman K, Eccles J. Clinical practice guideline management of blood borne viruses within the haemodialysis unit. *BMC Nephrol.* 2019;20:388.
8. Dawes C, Wong DTW. Role of saliva and salivary diagnostics in the advancement of oral health. *Journal of dental research.* 2019;98(2):133-41.

9. Navazesh M. Methods for collecting saliva. *Annals of the New York Academy of Sciences*. 1993;694:72-7.
10. Venkatapathy R, Govindarajan V, Oza N, Parameswaran S, Pennagaram Dhanasekaran B, Prashad KV. Salivary creatinine estimation as an alternative to serum creatinine in chronic kidney disease patients. *International journal of nephrology*. 2014;2014:742724.
11. Temilola DO, Bezuidenhout K, Erasmus RT, L Stephen, Davids, Holmes MRH. Salivary creatinine as a diagnostic tool for evaluating patients with chronic kidney disease. *BMC Nephrol*. 2019;20:387.
12. Lasisi TJ, Raji YR, Salako BL. Salivary creatinine and urea analysis in patients with chronic kidney disease: a case control study. *BMC nephrology*. 2016;17(1):10.
13. Sedkey R, Abd M, Kora A. Clinical significance of salive urea and creatinine levels in patients with chronic kidney disease. *Menoufia Medical Journal*. 2015;58:406-10.
14. Naing C, Wah Mak J. Salivary glucose in monitoring glycaemia in patients with type 1 diabetes mellitus: a systematic review. *Journal of Diabetes Metab Disord*. 2017;16:2.
15. Patel BJ, Dave B, Dave D, Karmakar P, Shah M, Sarvaiya B. Comparison and correlation of glucose levels in serum and saliva of both diabetic and non-diabetic patients. *Journal of international oral health*. 2015;7:70-6.
16. Hegde A, Shenoy R, D'Mello P, Smitha A, Tintu A, Manjrekar P. Alternative markers of glycemic status in diabetes mellitus. *Biomed Res*. 2010;21(3):252-6.
17. Gupta V, Kaur A. Salivary glucose levels in diabetes mellitus patients: A case-control study. *Journal of Oral and Maxillofacial pathology*. 2020;24(1):18.
18. Bhattacharyya A, Chandra S, Singh A, Raj V, Gupta B. Salivary glucose levels and oral candidal carriage in Type 2 diabetics. *Journal of oral biology and craniofacial research*. 2018;8(3):158-64.
19. Ragunathan H, Aswath N, Sarumathi T. Salivary glucose estimation: A noninvasive method. *Indian Journal of Dental Sciences*. 2019;11(1):25-7.