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مستويات الجلوكوز في لعاب مرضى داء السكري طريقة دقيقة للقياس

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Saliva Glucose Levels in Patients with Diabetes Mellitus: An Accurate Method for Measurement

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ABSTRACT

Background. In Iraq , around 1.2 million cases of diabetes are reported in 2015. Currently, diagnosis of diabetes is achieved by evaluating plasma glucose levels. Screening for diabetes in developing countries , however , is not easy because of limited resources, blood tests may be difficult to be performed . Relying on the less expensive tests available to predict high risk subjects for the development of diabetes is favored . Saliva offers some distinctive advantages as whole saliva can be collected non-invasively and by individuals with limited training. The present study estimated and correlated the plasma and salivary glucose levels in type 2 diabetic and non diabetic subjects aiming at validating saliva samples as routine method in dental chair side testing setup.



Method. The study population consisted of 200 subjects scattered on three groups: Group 1 consisted of diabetics with blood glucose level (BGL) $>200\text{mg/dl}$ and group 2 consisted of diabetics with BGL $130\text{-}200\text{mg/dl}$ based on their random plasma glucose levels. Group 3 consisted of healthy population as controls with BGL $<130\text{ mg/dl}$. Two ml of peripheral blood was collected for the estimation of random plasma glucose levels and unstimulated saliva was also collected for the estimation of salivary glucose levels.

Results. The salivary glucose levels were significantly higher in group 1 and group 2 diabetics when compared with controls. The salivary glucose levels show a significant correlation with plasma glucose levels between study populations, suggesting that salivary glucose levels can be used as a monitoring tool for predicting glucose level in diabetic patients.

Conclusion. The present study found that estimation of salivary glucose levels can be used as a noninvasive, painless technique for the measurement of diabetic status of a patient in a dental and primary health set up.

Key words : Diabetes mellitus , Plasma Glucose Levels , Saliva Glucose Levels , Enzymatic glucose oxidase peroxidase colorimetric Assay.

الملخص

تقييم تقنية قياس مستوى السكر في لعاب مرضى السكري بالمقارنة مع مستوى السكر في مصل الدم.

يستخدم اللعاب في تحاليل تشخيصية كثيرة لانه يعد ملائماً لهذه الاغراض المهمة. في هذه الدراسة تم اختيار عينة مرضى من 200 مريض واصحاء كسيطرة وقد قسمت على 3 مجاميع المجموعة الاولى تكونت من مريض سكري لديهم مستويات عالية من السكري (مستوى السكر غير مسيطر عليه) والمجموعة الثانية تكونت من مريض سكري متوسط اي مسيطر عليه اما المجموعة الثالثة فتكونت من اصحاء ليس لديهم داء السكري

تم اخذ عينات دم ولعاب من جميع العينة وقورن مستوى السكر في واللعاب حيث ظهر تطابق ممتاز في مستوى السكر في اللعاب والدم مما يدل على امكانية اللجوء الى اللعاب لتقييم و تشخيص مرض السكري في عيادات الاسنان كوسيلة بسيطة وعملية ونجح بتعميمها وتوسيع استخدامها على نطاق واسع



INTRODUCTION

Diabetes mellitus is a massive, growing, silent epidemic that has the potential to cripple health services in all parts of the world. Diabetes mellitus is a group of chronic diseases characterized by insulin deficiency, cellular resistance to insulin action, or both, resulting in hyperglycemia and other related metabolic disturbances. The disease is associated with serious complications of the eyes, kidneys, heart and blood vessels, and other organ systems, which may markedly impair quality of life and shorten the patient lifespan. Many people are affected by diabetes worldwide and the number is climbing steeply [1,2]. Currently, a diagnosis and monitoring of diabetes is achieved by evaluating plasma glucose levels. Blood is the most commonly used sample for laboratory diagnostic procedures, but it requires frequent invasion to vessels to collect the sample. It also causes unnecessary discomfort and mental trauma to patients; therefore, a much simpler and noninvasive technique for the diagnosis and monitoring of diabetes is very desirable [3]. Saliva offers some distinctive advantages. Whole saliva can be collected non-invasively and by individuals with limited training. No special equipment is needed for collection of the saliva fluid. Diagnosis of disease via the analysis of saliva is potentially valuable for children and older adults, since collection of the fluid is associated with fewer compliance problems as compared with the collection of blood. Further, analysis of saliva may provide a cost-effective approach for the screening of large populations. The collection and evaluation of the secretions from the individual salivary glands are primarily useful for the detection of gland-specific pathology, i.e. infection and obstruction. However, whole saliva is most frequently studied when salivary analysis is used for the evaluation of systemic disorders. The best two ways to collect whole saliva are the draining method in which saliva is allowed to drip off the lower lip. Another one is spitting method in which the subject spits saliva into a test tube. Different reagents are used to determine the content of saliva [4 , 5].In the literature, we encounter a controversy regarding the relationship between the



concentration of plasma glucose and salivary glucose. Several authors show that an increase in the concentration of glucose in saliva has to do with glycaemia; however, this relationship is not confirmed in other studies [6 , 7]. Some other studies have demonstrated the correlation of salivary glucose level (SGL) and blood glucose level (BGL) in diabetes [3]. The present study was aimed to estimate the correlation of plasma and salivary glucose levels in diabetic and non diabetic subjects, with special reference to age.

MATERIALS and METHODS

The study was carried out in 3 sets of samples in total 200 patients depending on their blood glucose level (BGL). Group I (more than 200 mg/dl of BGL), group II (more than 130-200 mg/dl of BGL), and group III (below 130 mg/dl of BGL) is healthy non-diabetic group, formed of age and gender matched healthy nondiabetic subjects. Group I and II considered as study population cases and group III as control population.

Verbal consent was obtained from each individual taking part in the study and a data sheet was completed detailing the person name, age, sex, and relevant medical history. The cases and control subjects were asked to come into the clinic in the morning between 8 am to 10 am, 2 mL venous blood was collected, in an ethylene diamine tetra acetic acid (EDTA) containing blood collection tube and stored. The patients were asked to wash their mouths with tap water and to spit two or three times, after which they were told to spit the saliva pooled in their mouths for the following 2 minutes into sterile sample collection container. The quantitative estimation of fasting plasma glucose (FPG) and fasting saliva glucose (FSG) levels were done by glucose oxidase method using enzymatic glucose oxidase peroxidase (GOD-POD) colorimetric assay kit (Biotic , Barcelona , Spain)



RESULTS

Table 1 shows that 50 subjects were found in group III (25 male and 25 female), the mean age was 41.08. 75 subjects were found in group II (42 male and 33 female), mean age was 52.65. 75 subjects were found in group I (40 male and 35 female), mean age was 53.71. However, no statistically significant difference has been observed Gender wise and age wise distribution of study subjects ($p < 0.57$ for gender wise distribution and $p < 0.67$ for age wise distribution, NS).

Table 2 shows comparison of salivary glucose and blood glucose levels between cases and control groups. The mean value of salivary glucose level versus blood glucose levels was 204 mg versus 209 mg for group I cases and 166 mg versus 158 mg for group II cases and control group it was 111 mg versus 118 mg. A statistically non-significant differences have been observed between cases and control groups.

DISCUSSION

Blood sample is the most common biologic fluid utilized for diagnosis and monitoring of diseases. However, whole saliva is frequently studied as an alternative for blood that can be useful even for diagnostic purposes. Whole saliva contains locally produced substances as well as plasma components that can be used for diagnosis of a variety of systemic diseases and understanding of their oral manifestations. Two of the advantages of salivary assessment are its non-invasive collection and cost effectiveness for screening large populations [8, 9]. Alterations of salivary composition in diabetic patients were documented. These biologic changes in diabetic whole saliva were different from one study to another that may be due to the diversity in sample selection criteria and study design [10 -12]. Diabetes is a globally wide spread disease consist of group of metabolic disorders that share the common underlying feature of hyperglycemia. Hyperglycemia in diabetes results from defects in insulin secretion, insulin action. Chronic hyperglycemia and the



attendant metabolic dysregulation may be associated with secondary damage in multiple organ systems, especially the kidneys, eyes, nerves, and blood vessels [2]. Various diagnostic devices are available in the market to measure the blood glucose level. However, in these products blood is taken as diagnostic body fluid. There is a necessity to establish a noninvasive procedure to determine the glucose level without taking blood.

Keeping the above in view, the present study was proposed at estimation of blood and salivary glucose level in diabetic and non diabetic subjects. The present attempt was designed to establish a noninvasive procedure to measure glucose level using saliva as the most easily obtainable specimens.

A correlation was observed between the salivary glucose level of diabetic and non diabetic study populations. These values of correlation proven by the Student t test ($p < 0.001$ Highly Significant) shown in Table 2. These results were in agreement with the studies done by many investigators[2 , 12].

We divided the patient group into three subgroups based on their plasma glucose level and compared the salivary glucose levels of those three groups. We found a statistically significant difference among the three groups. As such we can suggest that on the basis of our study that the range blood glucose level can correlate with salivary glucose level. Our results were in agreement with the data reported in [2, 11, 13]. However, no correlation were obtained with the study conducted [3, 6]. This difference could be due to the differences in method practiced by different study population group, selection criteria and also the method of collection of sample. Saliva indeed is a mirror of our blood as these bio fluids and their molecular components share many similarities. Realization of this fact and the possible utility of saliva as a diagnostic bio fluid using recent technological advances over the past decades has enabled many researchers to develop saliva based technology to detect the transition between health and disease [12]. As a diagnostic fluid, saliva offers distinctive advantages over serum because it can be collected noninvasively by



individuals with modest training. Furthermore, saliva may provide a cost effective approach for the screening of a large population. It is said that saliva lacks the drama of blood, sincerity of sweat and emotional appearance of tears but still the fact is that, it is the vital element that sustains life in the oral cavity [14]. The present attempt was designed to establish a non-invasive procedure to measure glucose level using saliva which is most easily obtainable. We know that glucose is present in the saliva of normal individuals; however, the mechanism of its secretion is still obscure. Both paracellular and intercellular pathways have been proposed, but this is still an hypothesis rather than an established theory. Many authors have tried to explain the increased glucose content in the salivary secretion of diabetic patients. Some studies tried to show that the salivary glands act as filters of blood glucose that are altered by hormonal or neural regulation [2, 4, 15]. Persistent hyperglycemia leads to microvascular changes in the blood vessels, as well as basement membrane alteration in the salivary glands. This leads to increased leakage of glucose from the ductal cells of the salivary gland, thereby increasing the glucose content in saliva [16]. This metabolic disease is a potential burden on both patients and society because of the high morbidity and mortality associated with infections and its renal, retinal and vascular complications.

Thus, it is essential to assess the magnitude of the problem and take steps for the early detection and control of DM with regular monitoring over glycemic control [17]. There are so many studies conducted. Not only glucose level there is also alteration of whole salivary constituents, such as salivary sodium, potassium, proteins, amylase, albumin and IgA, and a possible explanation was sought to the prevalence and severity of periodontal disease, dental caries in diabetic mellitus and role of saliva that brought about these changes [18, 19]. The routinely employed investigative procedures for glucose monitoring are invasive, but saliva can best serve as a valuable non-invasive diagnostic aid. Thus, the correlation between salivary and plasma glucose levels would be helpful in monitoring diabetes noninvasively.

Table 1- Gender and age distribution of study subjects

No	Male %	Female %	Age Range
Group I	40	35	29 – 88
Group II	42	33	27- 75
Group III	25	25	30 – 66
Total	105	93	

Table 2- Comparison of salivary glucose (SGL) and Blood glucose levels (BGL) between cases and control groups (Student t test):

Study population	Mean SGL (mg/dl)	Mean BGL (mg/dl)	SD t value
Group I Diabetics	204 mg	209 mg	Non-significant
Group II Diabetics	166 mg	158 mg	Non-significant
Group II Controls	111 mg	118 mg	Non-significant

CONCLUSION

There are definite changes in salivary composition, with increased levels of salivary glucose, total protein and enzymes in diabetic and non diabetic patients. The present study shows a significant positive correlation between the plasma and salivary glucose levels in the cases and study population.

The levels of glucose in plasma of diabetic patients could be reflected in saliva; hence the salivary glucose could be helpful for routine evaluation of diabetic patients. Detailed information on the possible influences of the salivary glucose levels and further studies which include random and postprandial glucose correlation would perhaps establish more definitively whether salivary glucose estimation would replace plasma glucose estimation



Such an event would be in the interest of the patient, since collection of salivary samples is an easy, safe and non-invasive procedure.

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