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RESEARCH ARTICLE

COMPARISON BETWEEN BLOOD-SALIVARY GLUCOSE LEVEL AND SALIVARY-LACRIMAL FLOW RATE IN DIABETICS AND NON DIABETICS

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ABSTRACT

Context: There is alarming rise in number of people with diabetes mellitus over these years. Saliva can offer a great value to detect the diabetes mellitus at an early stage if we are able to establish the positive correlation between blood and salivary glucose levels. Also there is decrease in the salivary and lacrimal flow rate seen in diabetic patients. **Aims:** This is a cross-sectional study undertaken with the aim to assess the correlation of salivary glucose level with blood glucose level and salivary and lacrimal flow rate in people with diabetes mellitus. Settings and Design: For investigations, 2 sets of samples of people with diabetes and the age and sex matched non-diabetic subjects were recruited. **Methods and Material:** Unstimulted salivary flow rate was measured by graduated syringe. The blood glucose level and salivary glucose levels in unstimulated whole saliva samples were analyzed using glucose oxidase method. Lacrimal flow rate was measured by Schirmmer's test. **Statistical analysis used:** Pearson's correlation coefficient test was applied to assess the correlation between salivary glucose level and blood glucose level. **Results:** The significant ($P < 0.05$) positive correlation of salivary glucose level and fasting blood glucose level was observed in people with diabetes in both the sets of samples. But there was no positive correlation found between salivary and lacrimal flow rate in people with diabetes in both the sets of samples. **Conclusions:** Although study suggests some potential for saliva as a marker in monitoring of diabetes mellitus, there are many aspects that need clarification before we reach to a conclusion.

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INTRODUCTION

Diabetes mellitus is a complex multi-system disorder characterized by a relative or absolute insufficiency of insulin secretion and/or concomitant resistance to the metabolic action of insulin on target tissues (Manfredi *et al*., 2004). Type 2 diabetes mellitus is the fifth most common chronic condition and the sixth leading cause of mortality among the elderly. The disease affects 9% of adults over the age of 65 years, and its prevalence has increased 30% to 40% during the past 20 years (Chavez *et al*., 2001). Glucose is a small molecule capable of moving easily through the membranes of blood vessels, passing from the blood plasma to the gingival fluid, via the gingival sulcus, reaching the saliva (Riaz, 2009). The increase in blood glucose in the diabetic patient could cause higher levels of salivary glucose with the consequent loss of homeostasis and greater susceptibility to diseases in the oral cavity (Vasconcelos *et al*., 2010).

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Collection of saliva is a non-invasive procedure and does not require any trained personnel or standard equipment. For this reason saliva can considered over serum as a diagnostic fluid. The chances of infection are lowered and disposal of associated wastes, poses a lesser health hazard. Furthermore saliva may provide a cost effective approach for screening large populations (Belazi *et al*., 1998; Ginsberg, 1992; Guevara, 2010; http:/www.healingwell.com/ - non invasive blood glucose monitors National institute of diabetes and digestive and kidney disease. National Institute of health, Bethesda). With regard to salivary flow rates, most studies have shown either decreased levels in diabetics or comparable levels among diabetics and healthy non-diabetics (López *et al*., 2003; Streckfus *et al*., 1994; Dodds, 1997; Collin, 2000; Collin *et al*., 1998). Diabetes is often associated with several significant ocular conditions, such as retinopathy, refractive changes, nerve palsies, glaucoma and macular edema. However, one of the most common ocular complications associated with diabetes is dry eye. Nearly 53% of people with diabetes experienced dry eye (Hom, 2010). Thus, the study levels in saliva and blood of patients with diabetes mellitus and non diabetic healthy individual, to determine the efficacy of saliva as a diagnostic aid. Also to correlate the lacrimal flow rate and salivary flow rate in diabetics and non diabetics healthy individuals.

MATERIALS AND METHODS

The study was conducted in the department of Oral Medicine, Diagnosis and Radiology, vasantdada Patil dental collage and hospital, Sangli. The patient participated in this study consisted of 75 subjects with diabetes and control group is consisted of 30 subject in the age group of 30 to 60 yrs. Age distribution and gender distribution of study subjects is summarized in [Table 1]. The patients were explained about the blood and saliva collection procedures in detail. The patients who were agreed to undergo the procedure were called in the next morning. The patients with pregnancy, lactation, chronic illness or taking any medications were not considered for the study. The patients were instructed to be fasting overnight and denture wearers were instructed not to wear denture till sample collection. The written informed consent was taken.

Blood sample collection: Patient was asked to seat comfortable in chair and resting the fully extended arm on padding. Tourniquet was tied around the upper arm to block venous flow and make vein prominent. Vein in the antecubital fossa was located and cleaned with a swab of cotton dipped in spirit and allowed it to dry. The skin was punctured by pushing in the needle firmly and steadily holding it at an angle of 10^o to 15^o to the skin. The skin puncture and vein puncture should be at different level. Approximately 2ml of blood was withdrawn. Tourniquet is then removed with left hand. Patient was then instructed to hold the swab and asked to flex the arm to maintain the pressure and raise the arm for a while above the level of the head to prevent seepage of blood through the puncture site. The collected blood was then transferred to sodium fluoride bulb by slowly pushing down the piston. The anticoagulant and blood was mixed by holding the bulb in the palm and rotating it. The collected blood sample was then stored at cool place at 2^o-8^oC. The collected blood sample was centrifuged at 3,000 rpm for 20min and clear supernatants were processed immediately for glucose estimation (Ranade et al.).

Salivary sample collection & salivary flow rate estimation: Patients were asked to rinse mouth with normal saline and asked to swallow or split the saliva which already present in the mouth. The samples collected in initial 30 seconds were discarded. The salivary sample collection was performed in morning between 8.00am- 11.00am with the patients sitting upright in a comfortable position. The samples were collected in a disposable plastic glass by expectoration method for 5min [FIGURE 1]. Thus the unstimulated saliva was collected (Panchbhai, 2012; Pal *et al*., 2003; Darwazeh *et al*., 1991; Aydin, 2007; Moore *et al*., 2001; Sharon *et al*., 1985). The unstimulated saliva was then measured by graduated syringe in terms of millimetre per minute (mm/min). The collected saliva was stored at 2-8^oC until used in glucose assay.

Blood and salivary glucose level estimation: Blood and Salivary glucose estimation were performed by GOD-POD method (Glucose GOD – PAP Biolab Diagnostics kit) TM. Briefly 1,000µl of reagent solution was pipette into each of 10µl of standard was added to the test tube marked "standard", followed by 10µl of test sample to the "Test" test tube. These were mixed well and all the test tube kept in an incubator at 37^oC for 10min before aspiration. Reagent blank was first aspirated in analyzer, followed by standard solution, for which the reading was noted and finally the test sample was aspirated and the reading was noted. Results were calculated and values were expressed as milligrams per decilitre (mg/dl).

Lacrimal flow rate estimation: Lacrimal flow rate was measured by schirmer's test. Patient was asked to seat comfortably on chair. Tear Touch schirmer strip TM was placed in the lower fornix at the junction of the middle and outer-third of the eyelid after folding it 5mm. of each eye. Subject was instructed to close eyes for 5min. Both the eyes are tested at the same time. After 5min, paper was removed and the amount of wetting from the fold is measured in terms of milliliters per 5 minutes [Figure 2] (Samar K. Basak; Leo, 1992; Pai *et al*., 2011).

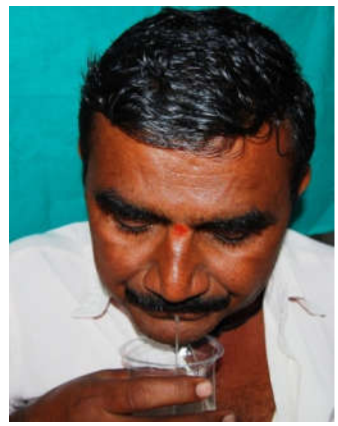

Figure 1. Collection of the saliva by expectorant method

Figure 2. Measurement of lacrimal flow rate by Schimmer's test

RESULTS

All statistical were performed using Microsoft Excel 2007 and SPSS (Statistical Procedure for Social Services) – version 16 statistical software programme. Comparison of control and study groups with respect to Fasting Blood Glucose levels, Fasting salivary Glucose level, Salivary Flow rate and lacrimal Flow rate was done by unpaired t test. The data were expressed as mean (standard deviation [SD] and in the entire tests P (probability) value < 0.05 was taken to be statistically

Table 1. Distribution of the groups studied according to sex and age the patients

	Experimental group	SD	Control group	SD
Male	39	45.67±8.62	17	45.29±8.44
Female	36	43.94±8.29	13	44.69±8.10

Table 2. General characteristics of the groups studied

	Experimental groups	Control groups	P value
Fasting blood glucose level	165.72±17.12	95.40±9.91	0.00001
Fasting salivary glucose level	19.61±3.02	10.04±3.32	0.00001
Salivary flow rate	0.34±10	0.33±0.10	0.4181
Lacrimal flow rate(RT)	17.36±2.36	16.53±2.94	0.1697
Lacrimal flow rate (LT)	17.32±2.78	16.37±2.81	0.1162

The present study comprised of 30 control and 75 freshly diagnosed diabetics in the age group of 30 -60. Out of a total of 30 samples in control group, 56.67% are males and 43.33% are females. The mean age of samples in control group is 45.03±8.16, in which male mean age is 45.29±8.44 and females is 44.69±8.10. Similarly out of a total of 75 samples in study group, in which 52.00% are males and 48.00% are females. The mean age of samples in study group is 44.84±8.45, in which male mean age is 45.67±8.62 and females is 43.94±8.29. The fasting blood glucose level in control group is 95.40±9.91 and in study group is 165.72±17.12. Fasting salivary glucose levels in control group is 10.04±3.32 and in study group 19.61±3.02. Salivary Flow rate in control group is 0.33±0.10 and in study group is 0.34±0.10. Lacrimal Flow rate in right eye in control group is 16.53±2.94 and in study group is 17.36±2.96. Lacrimal Flow rate in left eye in control group is 16.37±2.81 and in study group is 17.32±2.78. The results of distribution of blood glucose level and salivary glucose level, salivary flow rate and lacrimal flow rate in two sample groups are shown on [Table 2]. The significant positive correlation between salivary glucose levels and the fasting blood glucose levels was seen. Lacrimal flow rate [for right eye($t=-1.3829$, $p>0.05$) & left eye ($t=-1.5842$, $p>0.05$) and salivary rate($t=-0.8129$, $p>0.05$) at 5% level of significance is similar in both the 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 serum components that can be used for diagnosis of a variety of systemic diseases and understanding of their oral manifestations. Advantages of salivary assessment are its non-invasive collection and cost effectiveness for screening large populations (Kaufman, 2002). Mata *et al* reported alterations of salivary composition in diabetic patients (Mata *et al*., 2004). 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 (Kimura *et al*., 2001). Belazi *et al* showed higher salivary and serum glucose concentrations in children with insulin dependent diabetes mellitus (Belazi *et al*., 1998). Darwazeh *et al* demonstrated concentration of salivary glucose was related to blood glucose but there was no relationship with HbA1c (Pal *et al*., 2003). Kjellman detected higher levels of glucose in the whole saliva and gingival fluid of patients with diabetes mellitus. These differences may be due to the diabetes status and glycemic control (Kjellman, 1970). Reuterving *et al* demonstrated that salivary glucose concentration was lower during better glycemic control (Reuterving, 1987). Diabetes mellitus has been consistently documented to be associated with altered salivary composition and function (Thorstensson, 1989). In diabetic patients, salivary gland secretions are subjected to quantitative changes which lead to oral hard and soft tissue injuries. These changes will increase incidence of caries and periodontal diseases (Streckfus, 1994). In the present study the correlation between Fasting blood sugar and fasting salivary glucose levels, for different ranges in both the study group and control group was assessed. The means of all the study variable were found to be significantly more in the diabetic group as compared to the control groups ($p<0.001$). Review of the literature about salivary flow rate in diabetic patients has demonstrated some differences. In present study we found that there is no significant differences in salivary flow rate were seen between diabetics and non-diabetics. The observations were corroborating with the some previous studies (Chavez *et al*., 2001; Dodds *et al*., 1997; Aydin, 2007; Thorstensson *et al*., 1989). However, there are some studies that demonstrated significant decrease in flow rates in diabetics, which are contradictory to our result (Streckfus *et al*., 1994; Jukka *et al*., 1998). Negative effects of diabetes mellitus on the sympathetic and parasympathetic nervous system, microangiopathy, dehydration and hormonal changes may cause discrepancies in the salivary flow rate (Dodds *et al*., 1997; Collin *et al*., 1998). In addition, it was demonsstrated that neuropathies affecting the parasympathetic or sympathetic nervous system might have different effects on the flow rate and composition of saliva (Dodds *et al*., 2000). The occurrence of the dry eye disease and other ocular surface diseases is increased in diabetic patients (Grus, 2002). The most common dry eye symptoms reported by patients with diabetes are burning and foreign body sensation. Additional associated dry eye findings include tear film instability, a higher grade of conjunctival squamous metaplasia, lower goblet cell density, reduced corneal sensation and a reduced lipid layer of the tear film. Evidence even suggests a link between a family history of diabetes and symptoms of dryness. However, there are few studies which suggest that there is no change lacrimal flow rate in diabetics. Lacrimal flow rate examination includes Schirmer's test, break-up time, lipid layer thickness, fluorescein and rose bengal staining of the cornea, impression cytology, and a questionnaire. The ocular surface disease could be confirmed by performing multiple tear film tests. Among these tests Schirmer's test and Rose Bengal test have more diagnostic value in patients with type 2 diabetes as compared to Tear Film Break - up time test (Samar, ?; Rahman *et al*., 2007). Martin Goebbels Compared 86 consecutive insulin dependent diabetics with an age and sex matched group of 84 consecutive nondiabetic controls. There were no significant differences between diabetics and non-diabetic controls regarding the amount of aqueous tear flow as assessed by fluorophotometry and the break up time of the tear film. Both variables were found to be in a normal range both in the diabetic group and in the non-diabetic control group. However, Schirmer test values were found to be significantly decreased in the diabetic group when compared with the non-diabetic control group (Goebbels, 2000). There are some studies who found that there is decreased schirmer value of a diabetic patient as compared with control (Pai *et al*., 2011; Kenji *et al*., Dorgu *et al*., 2001).However, our study demonstrates that there is no change in schirmer's value of diabetics when compared non diabetics. Based on the observation of the present study, conclusions can be drawn 1) In present study, it has been established that there is a correlation between blood glucose levels and salivary glucose levels. Hence saliva can be used as screening method to detect diabetes. Because it can be collected non-invasively with modest training and without use of any sophisticated equipment and it is readily acceptable by patient. 2) In our study, salivary flow rate and lacrimal flow rate did not affect. Further study may be directed on the larger population and for longer period of time to evaluate the effect of diabetes mellitus on salivary flow rate and lacrimal flow rate.

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