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Salivary Glucose Levels and Its Correlation with Serum Glucose and Glycemic Status in Diabetic Patients

Diyabetli Hastalarda Tükrük Glukoz Seviyelerinin Serum Glukoz Seviyesi ve Glisemik Durum ile İlişkisi

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ABSTRACT

Purpose: Diabetes mellitus (DM) is an endocrine disease that is frequently encountered routinely by dentists. There is increased interest towards non invasive modes to diagnose this disease, one of which is Saliva. The aim of the study was to determine Salivary glucose levels in diabetic and healthy controls, to determine and compare salivary glucose levels with serum glucose in a group of diabetic subjects and matched controls and to study the correlation of salivary glucose levels and glycemic control status in diabetics and controls as determined by HbA1c values.

Material and Methods:-The study sample included 200 subjects, 120 with diabetes and 80 controls aged between 5-75 years. Samples of whole saliva and serum were obtained for determining salivary glucose level (SGL), Blood glucose level (BGL) and glycosylated hemoglobin (HbA1c). Serum and salivary glucose was assayed by use of Glucose Oxidase Peroxidase method. Glycosylated hemoglobin was determined by Ion Exchange Resin method.

Results:-Salivary glucose levels were significantly higher in diabetics than in controls. Significant positive correlation was found between SGL and BGL in diabetics as well as controls. No positive correlation was found between SGL and HbA1c, nor was any correlation found between SGL, age, sex, and duration of disease.

Conclusion:-Saliva can be used as a routine potential diagnostic tool in assessing diabetes mellitus, the most prevalent among Indian population. It is a simple and non invasive technique in screening and monitoring of this disease. Repeated painful pricks, hazard of getting infections, complications in hemophiliac patients and various other disadvantages that involve the blood tests currently used for diagnosis and monitoring of this widely prevalent Diabetes mellitus disease, can be replaced by non invasive tests involving Saliva, which is also a cost effective.

Key Words: Diabetes mellitus, Salivary Glucose level, Blood glucose level, Glycosylated

ÖZET

Amaç: Diabetes Mellitus (DM); diş hekimlerinin rutin çalışmalarında sıklıkla karşılaştığı endokrin sistemle ilişkili bir hastalıktır. Bu hastalıkta tükrük örneklerininde aralarında bulunduğu, non-invazif teşhise yönelik uygulamalara doğru bir eğilim vardır. Bu çalışmanın amacı diyabetli hastalar ile sağlıklı kontrollerin tükrük glukoz seviyelerini belirlemek ve bu iki grubun tükrük glukoz seviyeleri ile serum glukoz seviyelerini karşılaştırmak ve Diabetli vakaların oluşturduğu grup ile kontrol grubunun tükrük glukoz seviyesi ile ilişkili glisemik durumlarını,her iki grubunda HbA1c değerlerini göz önünde bulundurarak karşılaştırmak amaçlanmıştır.

Materyal ve Metod: Çalışma grubu, 5-75 yaşları arasında 120 diabetik ve 80 sağlıklı kontrol olmak üzere toplam 200 bireyden oluşmaktadır. Bu bireylerden alınan bütün tükrük ve serum örneklerinde; tükrük glukoz seviyesi (SGL), kan glukoz seviyesi (BGL), glikozile hemoglobin (HbA1c) değerleri belirlenmiştir. Kan (serum) ve tükrük glukoz seviyeleri

Glukoz Oksidaz Peroksidaz metodu kullanılarak tesbit edilmiştir. Glikozile hemoglobin (HbA1c) değeri ise Ion Exchange Resin yöntemi ile belirlenmiştir.

Bulgular: Tükrük glukoz seviyesi, diyabetik grupta kontrol grubuna göre önemli derecede yüksektir. Diyabetik ve kontrol gruplarında tükrük glukoz seviyesi (SGL) ve kan glukoz seviyesi (BGL) değerleri arasında önemli pozitif bir ilişki bulunmuştur. Diyabetik hastalarda tükrük glukoz seviyesi ile HbA1c değeri arasında ve SGL, yaş, cinsiyet ve hastalığın süresi gibi kriterler arasında herhangi bir pozitif ilişki bulunamamıştır.

Sonuç: Hindistan populasyonunda en yaygın gözlenen Diabetes Mellitus'un teşhisinde tükrük örneği potansiyel bir teşhis materyali olarak kullanılabilir. Tükrük örneği analizi hastalığın taranması ve takibinde kullanılacak basit ve non-invazif bir yöntemdir. Diabetes Mellitus' un teşhisinde ve gözleminde halen yaygın olarak kullanılan kan testleri, hemofilik hastalarda tekrarlayan ağrılı döküntüler gibi zararlı enfeksiyonları beraberinde getiren komplikasyonlar ve bunlar gibi pek çok dezavantaja sahiptir. Bu nedenle non-invazif tükrük testi kan testlerinin yerini alabilir. Aynı zamanda,tükrük testinin maliyeti de diğer yöntemlere kıyasla daha uygundur.

Anahtar Kelimeler: Diabetes Mellitus, Tükürük glukoz düzeyi, kan glukoz düzeyi, glikozile.

INTRODUCTION

Saliva is a complex fluid composed of a wide variety of organic and inorganic constituents that collectively act to maintain and modulate the oral environment. The composition and secretion of saliva is influenced by local as well as many systemic, hormonal, neurochemical, autonomic, drugs and metabolic factors. One such factor is Diabetes Mellitus (DM)[1,2].

Diabetes mellitus is a syndrome of abnormal carbohydrate, fat and protein metabolism that results in acute and chronic complications due to the absolute or relative lack of insulin[3]. Globally 140 million people are estimated to have DM. Primary prevention of the disease and the prevention of diabetic complications are of great practical importance[4].

Role of various markers like serum and salivary glucose, glycohemoglobin and other salivary parameters like amylase, proteins, lactoferrin, immunoglobulin, pH, electrolytes etc. have been consistently studied in disease progression, monitoring the control status and resulting clinical manifestations with contradictory results [4, 5, 6-11].

The literature however shows controversial findings with regard to the comparative values of blood and salivary glucose. Many authors reported higher salivary glucose levels in diabetics than in controls with positive correlation, whereas others have not supported this view[5, 10, 11]. Such investigations aimed mainly at exploring whether diabetic control could be monitored by a noninvasive method of salivary glucose measurement, the fact, however still a matter of controversies.

Glycosylated Hb, HbA1c has been used as diagnostic index for assessing the glycemic control of diabetes patients. It provides an estimate of average blood glucose level over preceding 30-90 day period[1]. Attempts by the various researchers to correlate SGL with HbA1c levels have shown contradictory results. Literature shows that serum glucose concentration in patients with DM reflects HbA1c levels with significant correlation[5, 12-14]. However, the same is not substantially applicable for SGL and HbA1c as evidenced by poor correlation between two in various past and recent studies [4, 15, 16].

Whole saliva has been shown to be important medium for diagnosis and monitoring of number of systemic conditions. It has distinctive advantages of being rapid, simple, cost effective, reduced non compliance, non invasive and that it can be collected by individuals with limited training. Analysis of saliva is proving to be potentially valuable for children, older adults as well as large population based studies. It has also been

suggested that determination of salivary components in DM patients may be useful in describing and further understanding the oral findings in this condition[17, 18].

Limited studies have attempted to investigate association of salivary glucose, blood glucose and HbA1c. Need was felt to explore the possibility of using saliva to reflect glucose concentrations in blood and at the same time, assessing the correlation with glycemic control of DM patients, with the aim to use saliva as noninvasive and painless modality in diagnosing this systemic disease. Considering the world wide increase in the incidence of diabetes, research directed towards the measurement of glucose by this simple non-invasive method may be useful not only in the diagnosis of disease, but also self monitoring by these paitents less invasive[5, 19].

Hence this project was undertaken with aims and objectives of investigating SGL and its correlation with BGL & HbA1c in diabetics and controls, thereby exploring its utility as a noninvasive method of monitoring this disease.

MATERIALS and METHODS

With approval from institutional ethics committee, this Case-control study was conducted on 120 DM subjects (aged 5-75 years) attending Diabetic OPD Clinic at S.N. Medical College and Hospital and P.M.N.M. Dental College and Hospital, Bagalkot. The control group comprised of 80 healthy individuals aged 5-75 years (age and sex matched) attending the dental hospital for regular dental check up. Criteria for inclusion was confirmed diagnosed cases of Type 1 DM and Type 2 DM , and for healthy controls, patients without any suggestion of diabetes mellitus and systemic diseases as confirmed by detailed history, not taking any systemic drug therapy, and whose serum glucose levels were within normal limits were included. Patients with history of smoking, alcoholism, salivary gland surgeries, receiving radiotherapy, pregnant women, under long term local and systemic drug therapy except (oral hypoglycemics and insulin), HIV- positive individuals and with systemic illness other than diabetes mellitus are excluded from the study. The entire procedure was explained to all the participants and informed consent was obtained from them.

Collection of samples

Saliva: Approximately 2 ml of unstimulated whole saliva is collected from study and control groups in a sterile graduated tube by spitting method as proposed by Navazesh et al 1993 (Kauffman) over a period of 5 minutes[20]. Saliva is collected in resting position after rinsing with distilled water between 8.00a.m and 10.30 a.m. Patient is asked not to eat or drink for 2 hours prior to collection. Saliva thus obtained is stored immediately in an icebox at temperature of -20ºCelsius, for no more than 2 hours or sent to the laboratory immediately. It is centrifuged at 2000 rpm for 5 minutes and subjected to analysis.

Serum: Under aseptic conditions 2 ml of patient's intravenous blood is obtained from median cubital vein of forearm, centrifuged at 2000 rpm, serum thus obtained is analyzed

Serum Glucose and Salivary Glucose determination: Serum and salivary glucose is assayed by use of Glucose Oxidase Peroxidase method- GOD- POD- Enzymatic Colorimetric method using test kit- UV- 1601 Visible Spectrophotometer, Shimadzu Corporation, Kyoto, Japan. SGL & BGL was determined in saliva & serum samples that were thawed and centrifuged. Briefly, 1,000 µl of reagent solution was pipetted into each of 3 test tubes labeled 'Blank', 'Standard' and 'Test'. Then, 10 µl of standard was added to the test tube marked as 'Standard', followed by 10 µl of test sample to the 'Test' test tube. After preparation of the tubes, these were mixed well for a few seconds in order to homogenize the saliva and enzyme reagent. After mixing well, the samples, standards and blank were incubated in a warm-water bath at 37°C for 5 min. The salivary glucose assay mixtures were prepared and

transferred to 1.5-ml cuvettes, and the absorbance was read with a UV spectrophotometer, at a wavelength of 505 nm. The absorbance values of standard and the sample against the reagent blank was measured[4, 19, 21]. Results were calculated and values were expressed as milligrams per deciliter (mg/dl) using the formula:-

$$\text{Glucose (mg/dl)} = \frac{\text{Absorbance of test-Absorbance of blank}}{\text{Absorbance of Standard-Absorbance of blank}} \times 100.$$

Glycohemoglobin (HbA1c) determination: HbA1c level is determined by use of test kit ERBA Diagnostic Manheim, GmbH, Germany by Ion Exchange Resin method.

Subjects with HbA1c values <6% are considered as normal. Diabetic subjects with HbA1c < 7% were considered as well controlled, 7%-8% as moderate control,> 8% were considered as poorly controlled[13].

All the samples were assayed on the same day of saliva collection. Analysis and interpretation of test values was done in Department of Pharmacology, H.S.K College of Pharmacy, Bagalkot.

Statistical Analysis:

t-test was performed to compare, between 2 independent groups. Karl Pearson's correlation coefficient was used to find out association between 2 qualitatively measured variable. Comparison of three groups with respect to a variable was done by one way ANOVA test. Pair wise comparison of three groups with respect to a variable was done by Newman-Keuls multiple post hoc procedure. Multiple regression analysis was done to confirm linear relationship between different variables such as SGL, BGL and HbA1c in a group. A P value of <0.05 is considered to be statistically significant. All these procedures were performed by using SPSS 16.0 version computer software for windows.

RESULTS

Table 1 shows distribution of study subjects by study groups and age groups with mean age. 56.67% of Type 1 DM group were males & 43.33% were females. 70% of Type 2 DM group were males & 30% were females. 65% of Control group were males & 35% were females. The mean duration of the disease in Type 1 DM was 9.6467 years and in Type 2 it was 6.25 years. There was no statistical significant difference (p=0.0659) between the mean duration of Type 1 DM & Type 2 DM.

Table 1: Distribution of study subjects by study groups and age groups with mean age

Groups	5-24yrs	%	25-44yrs	%	45-64yrs	%	65+	%	Total	Means
Type 1 DM	14	46.67	12	40.00	0	0.00	4	13.33	30	28.10
Type 2 DM	1	1.11	16	17.78	60	66.67	13	14.44	90	52.63
Control	5	6.25	17	21.25	54	67.50	4	5.00	80	47.85
Total	20	10.00	45	22.50	114	57.00	21	10.50	200	47.04

The mean SGL, BGL and HbA1c are shown in Table 2. SGL was in range of 0-19.74 mg/dl in diabetics combined, in controls it was 0-5.5mg/dl. BGL was in range of 85-520 mg/dl in diabetics combined, in controls it was 74-147mg/dl. HbA1c was in range of 5.4%-18.7% in diabetics combined, in controls it was 3-6.4%.

Table 2: Mean and SD of SGL (mg/dl), BGL (mg/dl) and HbA1c (%) by three groups (Type 1 DM, Type 2 DM and Control)

Groups	SGL (mg/dl)		BGL (mg/dl)		HbA1c (%)	
	Mean	SD	Mean	SD	Mean	SD
Type 1 DM	2.90	1.36	232.03	84.10	7.75	2.26
Type 2 DM	2.90	3.37	201.46	94.83	7.96	1.52
Control	0.64	1.23	115.78	21.04	4.77	0.92
Total	2.00	2.68	171.77	86.22	6.65	2.12

There was statistically significant difference (P=0.0000, F=20.4790) in SGL between the three groups (Type 1 DM, Type 2 DM and Control), between the SGL of Type 1 DM & control (P=0.0000), & between Type 2 & control (P=0.0000), in BGL between the three groups P=0.0000, F-value=41.5711(Type 1 DM, Type 2 DM and Control), between the BGL of Type 1 DM & control (P=0.0000), Type 1 DM & Type 2 DM (P=0.0308) & between Type 2 DM & control (P=0.0000).No statistically significant difference was found between SGL of Type 1 DM and Type 2 DM (P=0.9988)

There was also statistically significant difference (P=0.0000, F-value==110.7584) in HbA1c between the three groups (Type 1 DM, Type 2 DM and Control), between the HbA1c of Type 1 DM & control (P=0.0000) & between Type 2 DM & control (P=0.0000), between the SGL of diabetics & control (P=0.0000) BGL of diabetics & control (P=0.0000), HbA1c of diabetics & control (P=0.0000). No statistically significant difference was found between HbA1c of Type 1 DM and Type 2 DM (P=0.4492)

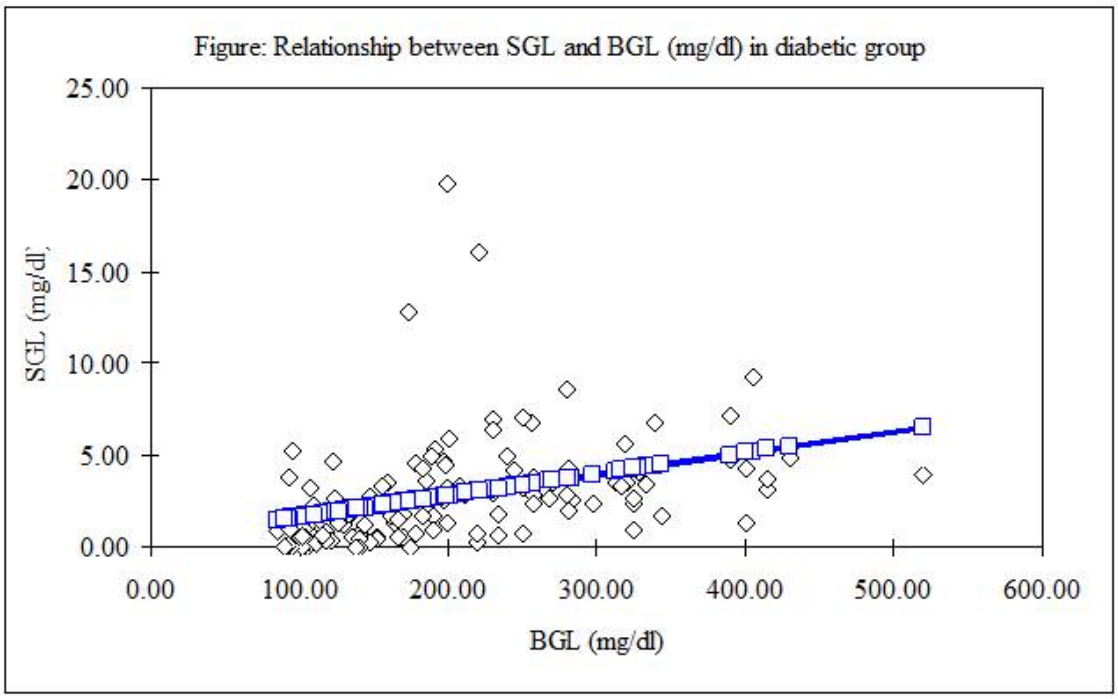
SGL was 3.02±2.91 mg/dl and 2.66±3.24mg/dl in combined diabetic males and female patients respectively. There was no statistically significant difference between the SGL of males & females in diabetics with respect to SGL (P=0.5360), BGL (P=0.4768) and HbA1c (P=0.7607). There was no significant correlation between age and SGL in Diabetic group combined (r=0.0132, p=0.8861), Type 1 DM (r=0.0742, p=0.6967), Type 2 DM (r=0.0079, p=0.9412) & control (r=0.0644, p=0.5702) using Karl Pearson's correlation technique.

Correlation among SGL, BGL, and HbA1c in diabetics, Type 1, Type 2 and controls is shown in Table 3, Figure 1. There was no statistically found correlation (P>0.05) between duration of disease with SGL, BGL and HbA1c in Diabetics combined, Type 1 DM, & Type 2 DM groups.

Table 3: Correlation among SGL, BGL and HbA1c in DM, Type 1, Type 2 and Control

Group	Group	SGL (mg/dl)	BGL (mg/dl)	HbA1c (%)
Diabetic	SGL (mg/dl)	1.0000		
	BGL (mg/dl)	0.3617a	1.0000	
	HbA1c (%)	-0.0129	-0.0076	1.0000
Type 1 DM	SGL (mg/dl)	1.0000		
	BGL (mg/dl)	0.7147a	1.0000	
	HbA1c (%)	-0.4376a	-0.3899a	1.0000
Type 2 DM	SGL (mg/dl)	1.0000		
	BGL (mg/dl)	0.3372a	1.0000	
	HbA1c (%)	0.0681	0.1681	1.0000
Control	SGL (mg/dl)	1.0000		
	BGL (mg/dl)	0.4498a	1.0000	
	HbA1c (%)	0.0769	-0.0388	1.0000

Positive correlation (r value)[a], p<0.05



Based upon the collected data, the subjects were divided into 3 categories based upon their HbA1c values as Good (n=35), Moderate (n=33), and Poor (n=52). There was no statistically significant difference (P=0.2254) in SGL of three categories of HbA1c in diabetics. Multivariate regression analysis confirmed the significant linear relationship between SGL & BGL but not with HbA1c (Table 4)

Table 4: Multiple regression analysis of SGL with BGL and HbA1c in Diabetic group

Independent variables	Beta value	SE of Beta	Regression coefficient	SE regression coefficient	t-value	p-level
Intercept			0.6103	1.3420	0.4548	0.6501
BGL	0.3616	0.0862	0.0116	0.0028	4.1961	0.0001[b]
HbA1c	-0.0102	0.0862	-0.0176	0.1490	-0.1179	0.9064
R=0.3618, R^2=0.1309, 6 Adjusted R^2=0.1160, F=8.8147 p<.00027 Std.Error of estimate: 2.8081						

$p<0.05$[b]

DISCUSSION

Whole saliva is frequently studied as an alternative for blood that can be useful for monitoring the disease[4,7,16,17,22,23]. The extent of compositional alterations and flow of saliva with their clinical significance have been explored by many investigators in DM[6, 2, 8, 9, 11] . Most of the studies were carried on Type 2 DM patients[4,19], whereas some have included only type 1 DM patients in their study[15, 17,24] . In comparision to study done by Vaziri et al. and Darwazeh et al. this study reports slightly higher percentages for Type 2 DM and lower for Type 1 DM[16, 22].This can be explained by the fact that Type 2 being more prevalent than Type 1 DM.

The use of “Spitting technique” for salivary collection and “unstimulated whole saliva” for estimation of glucose analysis have been widely advocated in literature[17, 25] whereas Forbat et al., Englander et al., Andersson et al. and Sharon et al. estimated parotid saliva for glucose evaluation[10, 11, 26, 27]. It has been argued that whole salivary samples collected by spit technique represent whole mouth fluid contributed by secretions from major and minor salivary glands and potentially gingival crevicular fluid and capable of representing the salivary glucose which follows the threshold mechanism. Apart from alterations in the permeability of the basement membrane changes in DM, it is possible that a part of the registered salivary glucose content originates from gingival fluid. For a general assessment of salivary function, unstimulated whole saliva collection is the recommended method of collection. In agreement with above views we adopted the spitting technique for salivary collection and whole saliva as a medium of analysis for glucose in the present study[1,16 20,28].

Our finding of increased glucose concentrations in mixed saliva of diabetic patients compared with non-diabetic individuals is consistent with that reported in literature using the same type of saliva sample[5, 7, 16]. There is possibility of Saliva substituting for blood in lab tests for the diagnosis of illness[28], for example, in determining glycemia in the monitoring of DM, thereby being a non-invasive procedure and allowing multiple samplings. As glucose concentration is elevated in diabetics, it is important to investigate and compare the SGL and BGL in diabetics and nondiabetic patients[19].

Various methods have been mentioned in the literature regarding the SGL estimation- Somogyl, korteum, GOD-POD, GOD-PAP, etc were some of them[22, 23, 25]. However Glucose oxidase method by UV enzymatic colorimetric- using UV spectrophotometry has been considered as most sensitive method with sensitivity detection level for glucose as high as 102.2% and it is argued that it could measure a minimal salivary glucose concentration of 0.2mg/dL. Further it is observed that transparency of saliva after centrifugation is

convenient because the interference with colorimetric methods is disabled making it a reliable method. In agreement with the various authors we employed GOD-POD method using UV spectrophotometry in automated analyzer[16,25].

The SGL in diabetics and controls have been reported by various authors[25, 29]. The present results confirm that the glucose concentrations in saliva of both type of DM were higher (P=0.0000) in diabetic patients than in healthy control subjects which is similar to other studies[16,19,23]. However Sharon et al. found that the glucose concentration in whole saliva was similar in diabetics and controls whereas it was significantly higher in the parotid saliva of the diabetic patients than controls (p<0.02). Vaziri et al. reported no significant differences in the SGL of Type 1DM (P=0.88) and Type 2 DM (P=0.19) with control groups, which contradicts our observation. However, there is divergence with respect to absolute values of SGL determination for DM. It is believed that such differences can be due to differences in methods utilized to determine glucose and in saliva collection and sample designs[11,22].

The SGL of Type 1 patients in our study is slightly higher than that reported by Lopez et al. and slightly lower than Karjalainen et al and Belazi et al. SGL of Type 2 DM in our study was in the range to that reported by Sreedevi et al, Shashikumar R et al. Our observation was similar to done by Vaziri et al and Darwazeh et al who reported no significant relation of SGL with types of diabetes[16,22].

In this study, glucose was detected in the unstimulated whole saliva of controls, as reported by Darwazeh, Ben- Aryeh et al. [16, 30]. The Mean SGL of control group in our study was similar to values observed by Darwazeh et al. Belazi et al. and Campbell et al. It was slightly lesser than that reported by Shashikumar R et al. (2.6mg/dl)[16,17,31]. Shashikumar R et al. reported significant higher level of SGL in non diabetic patients, the finding higher than that reported by other authors as well as in the present study[4]. This was attributed to carbohydrate-rich dietary pattern of the Indian population. Apart from their views the possible explanation for these differences may be the choice of certain study designs, the diversity of methods and criteria for selecting the samples[28].

In our study mean BGL in Type 1 DM was similar to that observed by Belazi et al., and Karjalainen et al[17, 24]. We reported Type 2 DM mean BGL similar to Vasconcelos et al. & Sharon et al[11,19]. The literature reports range of BGL values for Type 2 DM as 205-490mg/dl[18]. These diversities could be attributed to certain factors like capillary versus venous sampling, random versus fasting blood and various modes of glycemic control by patients in different studies.

We found statistically significant differences between BGL of Type 1 DM and controls, between Type 1 DM and Type 2 DM BGL levels & between Type 2 DM and control BGL levels. Similar observations were made by Sreedevi et al. (P<0.01) for diabetes and control group. In our study we observed no significant difference in BGL between either sex of diabetics and controls. Soares et al had similar findings with respect to control group[18, 28].

The finding of correlation between BGL and SGL of DM group corroborates those of Shashikumar et.al, Sreedevi et al, Darwazeh *et al.*, Belazi *et al.* and Amer *et al*.[4,5,16-18]. However, it differs from the results of Ben-Aryeh et al., Forbat et al., Carda et al, Lopez et al, Sharon et al, Vasconcelos et.al. who reported negative correlation between SGL and BGL[7,10,11,15,19,30]. Whether this reflects the sensitivity of the test used or other factors need further investigation. In our study “Multivariate analysis” showed that SGL significantly correlated with BGL (P=0.0001).

A decrease in mean salivary glucose was observed by Karjalainen et al. in the newly diagnosed Type 1 DM cases after 2 weeks on insulin treatment, while blood glucose levels decreased significantly. Salivary glucose levels and mean blood glucose levels in the hyperglycemic state were correlated. Magnitudes

of the decrease in salivary glucose and blood glucose levels also correlated with each other. These results suggest that blood glucose levels are related, to certain extent, to salivary glucose levels[24].

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. 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[11]. Factors other than elevated blood glucose may lead to elevated salivary glucose such as increased basement membrane permeability of the parotid gland and those originating from gingival fluid[4].

We observed significant correlation between SGL and BGL in controls. Darwazeh et al. reported significant correlation (r=0.33, p<.05) between SGL and BGL of diabetes but no such relationship was apparent for control subjects (r=0.21, p>0.05).In disagreement with report of ours, Shannon et al. observed no correlation between BGL and SGL of whole saliva and parotid saliva in healthy controls. However Sreedevi et al. reported a strong correlation between SGL and BGL in controls(r=+0.74). Soares et al. reported that the concentrations of SGL did not present any statistically significant correlation with capillary glycemia in healthy adults (P=0.78)[16, 18, 28, 32].

We found no statistically significant difference (p=0.536) mean SGL in males and females in diabetic group. Mehrotra and Chawla found higher SGL in female patients than male patients of diabetic group. They also reported that SGL increases with increasing age in female DM patients only[23]. Jurysta et al. also showed that SGL of males and females failed to differ significantly in DM. Darwazeh et al. reported the similar findings as in our study with regard to age and gender (p>0.06, r=0.22) . We agree with Darwazeh et al. who reported no significant correlation between SGL and duration of disease (r=0.026)[16, 29].

The HbA1c levels did not show significant correlation with SGL in diabetics combined, Type 2 DM and controls in our study. The similar observations were done by Darwazeh et al (r=0.095), Maria Lopez et al., probably reflecting the fact that it represents an average value for 3 months. Shashikumar R et al. confirmed that there was no significant linear relationship between Unstimulated salivary glucose and Stimulated Salivary glucose, with HbA1c by Mulivariate regression analysis. The study agrees with authors observation as far as unstimulated whole salivary glucose values[4 5,16].

A significant –ve correlation was found in Type 1 DM between HbA1c and SGL, and also between BGL and HbA1c which may be attributed to fluctuating BGL in these patients, fluctuations in metabolic control, type of treatment regimen and fluctuations in BGL in these patients. Similar findings were reported by Karjalainen et al. who found no correlation between SGL levels and HbA1 values in the long term Type 2 DM cases. In authors view, short-lasting hyperglycemic states- not reflected in HbA1c values- may alter the glucose levels and thus responsible for poor correlation between SGL & HbA1c. Carda et al. observed that only diabetic individuals with fasting glycemia of 180 mg/dl and glycosylated hemoglobin higher than 8%, showed elevated salivary glucose, compared to those patients with poor metabolic control [7, 24]. There was no significant correlation between BGL and HbA1c in diabetic group combined, in Type 2 DM, and in control group.

Reuterving et al demonstrated that SGL was lower during better glycemic control. Although no statistically significant difference (p=0.225) was found in our study between SGL and HbA1c in DM, mean SGL were higher in moderate control (3.5176mg/dl) followed by poor (2.941mg/dl) and good controlled (2.26mg/dl) DM patients, the fact which cannot be ignored[33]. Further studies are

required to explore this aspect of SGL reflecting the HbA1c levels.

CONCLUSIONS

Based on the results obtained in the present study, it can be concluded that: 1) DM influences the concentration of salivary glucose; 2) SGL is directly influenced by glycemia, and thus can be used to monitor BGL in diabetics; 3) HbA1c cannot be reflected by measuring SGL in diabetic patients.

In the light of these results the present study supports the use of saliva as a diagnostic fluid in DM, the common systemic ailment most prevalent in Indian population, where it would especially prove valuable. As the numbers of DM patients are being increasing recently, a simple and non-invasive screening examination should be used universally and the present study contributes to broadening the understanding of the field of BGL monitoring. When an easier method than invasive versus self monitoring of blood glucose is evaluated as reasonable, the DM patients will be free from some burden. Thus, a saliva glucose method and/or modality would be helpful.

Further large sampled studies are required to study the relationship between SGL, BGL and HbA1c in DM patients so as to standardize a simple and non invasive technique in screening and monitoring of this disease.

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Conflict of interest page:- All authors have no conflict of interest.

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