Correlation of Salivary Glucose level with Blood Glucose Level in Patients with Diabetes Mellitus

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ABSTRACT

Diabetes Mellitus (DM) is a systemic disorder characterized by hyperglycemia either due to insulin resistance or insulin deficiency. This can lead to many serious life-threatening complications if not managed properly by regular monitoring of glycemic status. Prevalence of fear of needles in the society make people non-compliant to regular monitoring. Thus, there is a need for a non-invasive method for determining the glycemic status of the individual. Salivary Glucose has the potential to be one such tool. This study aimed to find whether a correlation between fasting blood glucose levels and fasting salivary glucose levels could be established in diabetic and non-diabetic individuals. 50 patients with DM and 50 patients without DM were studied. 5 ml of venous blood and 5 ml of unstimulated saliva after overnight fasting were collected from each participant and processed using standardized enzymatic methods. The data was analyzed using SPSS software. There was a strong and very significant positive correlation (r=0.800, p=0.001) between fasting salivary glucose levels and fasting blood glucose levels in patients with DM whereas the correlation was weak and insignificant in patients without DM (r=0.111, p=0.441). The cut off value for diagnosing DM was found to be > 2.2mg/dl with 100% specificity and 100% sensitivity.

INTRODUCTION

Diabetes mellitus (DM) is a globally spread metabolic disorder, which is characterized by elevated blood glucose level leading to multiple organ damage if not controlled properly. The worldwide prevalence of DM has risen dramatically over the past decades from an estimated 30 million cases in 1985 to 463 million people in 2019. India has the world’s second largest diabetic population after China (Anon and IDF, 2020). Diabetes mellitus is not just a health crisis, but a global societal catastrophe (Carruth and Mendenhall, 2018). Due to its chronic nature, diabetes mellitus can cause devastating personal suffering and drive families
into poverty. Countries, especially those in low and middle income groups, are struggling to meet the financial burden due to the disease and its complications (Moucherad et al., 2019).

The metabolic dysregulation associated with diabetes mellitus causes secondary pathophysiologic changes in multiple organ systems. It is a major cause of end-stage renal disease, nontraumatic lower limb amputations, and adult blindness worldwide. It also predisposes to cardiovascular diseases (Powers, 2012). However, most of the microvascular complications can be prevented with proper control of glycemic levels. In this scenario, where early treatment is potentially lifesaving, more than 47% of the diabetic population worldwide remain undiagnosed. This potentially worsens their quality of life and outcomes (Anon and IDF, 2020).

Studies have documented the importance of glycemic control in delaying the onset and decreasing the incidence of both short and long-term complications of DM (LeRoith and Smith, 2005). Glycemic levels are currently monitored either by serum or by urine sample (Kakkad et al., 2015). Blood sugar estimation remains the current gold standard in the management of DM (Ladgotra, 2016). However, as it is a painful procedure for the patients, especially pediatric and geriatric group might be anxious towards it. There is always a minimal risk of infection even with aseptic precautions while withdrawing the blood and there is a need for a skilled person to withdraw blood (Smirti, 2016). Fear and anxiety to needles may result in non-compliance with health care procedures, such as performing blood tests; hence a much simpler and non-invasive technique for the diagnosis and monitoring of diabetes is very desirable (Sokolowski et al., 2010). One such technique which has been evaluated recently is estimation of salivary glucose levels.

Saliva is a unique biological fluid composed of a variety of electrolytes like sodium, potassium, calcium, magnesium, bicarbonate, and phosphates. It also has immunoglobulins, proteins, enzymes, mucins, and nitrogenous products, such as urea and ammonia (Humphrey and Williamson, 2001). It is already being used to study systemic conditions by identifying antibodies, unconjugated steroids hormones and certain drugs in it (Amer et al., 2001). It is also now emerging as a diagnostic tool for early detection of multiple systemic and oral diseases (Roi, 2019).

Previous studies have suggested that elevated salivary glucose may be due to easy diffusability of the molecule because of its small size or may be due to the membranous defect in the semi permeable membrane caused by hyperglycemia in patients with diabetes (Bhattacharyya, 2018; Indira, 2015). However, the extent of the alteration in the composition of the fluid and its clinical significance has not been well established in all subsets of population. Saliva, as a diagnostic fluid offers distinctive advantages over serum as it can be collected non-invasively with modest training and without use of any sophisticated equipment overcoming many of the shortfalls associated with blood sampling (Harish and Shantharam, 2019). Also, the disposal of associated waste doesn’t possess any major or untoward health hazard (Karki et al., 2014; Khayamzdeh et al., 2017). Our study was designed to find the correlation between fasting salivary glucose level (FSGL) and fasting blood glucose levels (FBS) in patients with DM and patients without DM.

**METHODOLOGY**

Institutional Ethics Committee clearance was obtained. The sample size was calculated to be 48 in each group using data from an earlier study (Harish and Shantharam, 2019) and allowing for a power of 80% and alpha error of 5% for a two sided analysis. A cross sectional study was conducted among patients admitted in the inpatient wards of the Department of General Medicine of a tertiary care hospital. Patients of either sex who were above 18 years of age were eligible for the study after providing informed consent. Diabetic patients were identified as patients who had at least one reading of HbA1c of above 6.5% in the last 3 months. Patients who were admitted in the wards for other complaints and whose fasting blood sugars were less than 100 mg/dL were included in the non-diabetic group. Patients with history of salivary gland surgeries or salivary gland disorders like Sjogren's syndrome, patients who had undergone chemotherapy or radiotherapy of head and neck cancer, patients on treatment with immunosuppressants or steroids, patients who had a habit of alcohol abuse, smoking, betel nut chewing or using any smokeless forms of tobacco or unable to provide a salivary sample were excluded from the study.

After obtaining informed consent from the participants, demographic details and history regarding DM, duration of DM, associated risk factors, family history and any associated illness was obtained. Unstimulated whole saliva and blood samples from each participant were collected after overnight fasting of minimum 8 hours. Unstimulated whole saliva samples were collected from the participants in a clean sterile container by spitting method. The
participants were instructed to rinse the oral cavity using plain water two or three times and to sit upright in a comfortable position. They were then asked to hold the saliva secreted in oral cavity without swallowing for 5 minutes and then asked to spit the pooled saliva into the sterile plastic container. Following the collection of a saliva sample, 5ml of venous blood was collected from the median cubital vein of forearm in a sterile test tube with fluoride as the preservative.

The collected salivary samples were centrifuged and the clear supernatant produced was processed immediately for quantitative estimation of glucose by enzymatic methods using glucose oxidase – peroxidase (GOD – POD) method in a semiautomated analyzer. The collected blood samples were processed immediately for quantitative estimation of glucose by using hexokinase method in a fully automated analyzer.

The Pearson's correlation coefficient between FBS and FSGL was 0.80 and statistically significant (p < 0.001) in Group 1 while it was 0.11 and statistically not significant (p=0.44) in Group 2. The scatter plot diagram for the two groups (Figures 1 and 2) are shown. Using FSGL as the independent variable (X) and FBS as the dependent variable, the line of best fit was found to be Y = 117.1 + 10.75 X.

ROC analysis was done after categorizing the data with the cut off value 2.55 mg /dl obtained from a previously conducted study (Karki et al., 2014). The cutoff value of fasting salivary glucose level for diagnosing DM was found to be > 2.2 using ROC curve with 100% sensitivity and 100% specificity. The area under the curve was 1.00.

There was a highly significant and strong positive correlation between FBS and FSGL in patients with DM (r=0.800, p=0.001) while there was no significant correlation in the non-diabetic group. This was similar to the findings of the study done by (Azizi and Modaberi, 2014) who studied 75 diabetic and 75 non diabetic patients. There also a significantly high positive correlation between FBS and FSGL in patients with DM (r=0.90) was shown while no significant correlation was demonstrated in the non-diabetic group. The mean salivary glucose in those patients with DM was 1.4 ± 0.2 mg/dl and mean blood glucose was 247 ± 24.2 mg/dl. (Azizi and Modaberi, 2014). Similarly (Ladgotra, 2016) also found a significant correlation (p=0.018) between serum and salivary glucose level in participants with DM and insignificant correlation (p=0.349) between serum and salivary glucose level in participants without DM (Ladgotra, 2016).

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RESULTS AND DISCUSSION

The study population consisted of 100 participants, 50 patients with Type 2 DM (Group 1) and 50 patients without DM (Group 2). The Age Sex distribution of the study participants is shown in Table 1. The median age was 55 years (IQR: 45 – 61) in Group 1 and was 53.5 years (IQR: 42 – 63) in Group 2. The mean BMI was 22 ± 3.3 in Group 1 and 21 ± 2.4 in Group 2 and the difference was not statistically significant. In Group 1, 22% (n=11) of patients had diabetes for more than 15 years, 32% (n = 16) had diabetes for 10 – 15 years, 24% (n = 12) had diabetes for 5 – 10 years and the remaining 22% (n = 11) had diabetes for less than 5 years. 42% (n = 21) of patients were on Insulin therapy alone, 34% (n = 17) were on oral anti diabetic drugs, 18% (n = 9) were on oral anti diabetic drugs along with Insulin and 6% (n = 3) were on lifestyle modification alone.

The mean Fasting Blood Sugar (FBS) in patients with DM (group 1) was 173.7 ± 68.6 mg/dL and in patients without DM (group 2) was 88.2 ± 9.9 mg/dL. The mean Fasting Salivary Glucose Levels (FSGL) in patients with DM was 5.3 ± 5.1 mg/dL and in patients without DM was 1.4 ± 1.0 mg/dL. The Pearson’s correlation coefficient between FBS and FSGL was 0.80 and statistically significant (p < 0.001) in Group 1 while it was 0.11 and statistically not significant (p=0.44) in Group 2. The scatter plot diagram for the two groups (Figures 1 and 2) are shown. Using FSGL as the independent variable (X) and FBS as the dependent variable, the line of best fit was found to be Y = 117.1 + 10.75 X.

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Table 1: Age Sex distribution of the study participants

<table>
<thead>
<tr>
<th>Age</th>
<th>Group 1 Sex Distribution</th>
<th>Group 2 Sex Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 years</td>
<td>Male: 3</td>
<td>Female: 0</td>
</tr>
<tr>
<td>30 – 50 years</td>
<td>Male: 4</td>
<td>Female: 12</td>
</tr>
<tr>
<td>50 – 70 years</td>
<td>Male: 15</td>
<td>Female: 12</td>
</tr>
<tr>
<td>&gt; 70 years</td>
<td>Male: 3</td>
<td>Female: 1</td>
</tr>
<tr>
<td>TOTAL</td>
<td>25</td>
<td>25</td>
</tr>
</tbody>
</table>

patients with DM (r=0.941) and patients without DM (r=0.945). The mean FSGL was 15.158 ± 1.78 mg/dl in patients with DM and 3.176 ± 1.28 mg/dl in patients without DM whereas the mean FBS levels were 152.70 ± 14.94 mg/dl and 68.20 ± 14.63 mg/dl respectively. The mean salivary glucose levels in their study were comparatively much higher in comparison to the present study. (Kakkad et al., 2015). Similarly, (Dhanya and Hegde, 2016) also found significant correlation between serum glucose and salivary glucose in patients with DM and patients without DM (r = 0.88 and 0.63 respectively). The mean salivary glucose level in those patients with DM was 8.47 ± 4.20 mg/dl and in patients without DM was 1.20 ± 0.6 mg/dl whereas the mean FBS were 136.30 ± 28.58 mg/dl and 97.78 ± 6.39 mg/dl respectively (Dhanya and Hegde, 2016). (Harish and Shantharam, 2019) also showed significantly high correlation in uncontrolled DM (r=0.917), controlled DM (r=0.748) and in healthy controls (r=0.841) (Harish and Shantharam, 2019). (Agarwal, 2013) also showed a correlation between FBS and FSGL in both diabetic (r=0.40) and non-diabetic patients (r=0.58) (Agarwal, 2013). In the present study, a correlation between FSGL and FBS could not be identified in non-diabetic patients. In contrast to the above cited studies and the present study, Indira et al. found no significant correlation between FBS and FSGL in their study. (Indira, 2015)

ROC analysis was done after categorizing the data with the cut off value 2.55 mg /dl obtained from a previously conducted study (Karki et al., 2014). In that study, the cut off value set by ROC curve was > 2.55mg/dl at which sensitivity was 86.7% and specificity was 90% (AUC =0.934). In the present study, the cutoff value of fasting salivary glucose level for diagnosing DM was set by ROC curve to be > 2.2mg/dl at 100% sensitivity and 100% specificity (AUC = 1.00). Khayamzdeh et al. found a cut-off value of unstimulated salivary glucose for the diagnosis of IDDM of 1.05 mg/dl with 75% sensitivity and 60% specificity. (Khayamzdeh et al., 2017). (Kumar et al., 2014) showed FSGL greater than 6.8 mg/dl as the diagnostic criterion for DM with 83.3% sensitivity and 100% specificity. (Kumar et al., 2014).

CONCLUSIONS

From the findings of the present study we could conclude that saliva can be employed as a screening and monitoring tool for DM. Analyzing salivary glucose can be a non-invasive and cost effective approach for the screening and diagnosis of diabetes mellitus. It can be used in large screening programmes as collection of the sample can be done with modest training. Early detection of diabetes mellitus would become much easier with such a non-invasive approach. However, the study also has certain limitations. The study had a relatively small sample size which necessitates further studies in large populations to establish the reference range for salivary glucose levels. The larger studies can also help identify the exact cut off for diagnosis of diabetes in a more accurate way as current knowledge is still unable to identify the ideal diagnostic range. There is also a need for developing a standardized procedure for storage and transport of the salivary sample. If these are achieved then, the management of diabetes mellitus will see a whole new paradigm.

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Conflict of Interest

The authors declare that they have no conflicts of interest for this study.

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