A Review on Saliva and Serum Lipid Profile Levels in Type 2 Diabetics

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ABSTRACT

Saliva, a biologic fluid secreted by salivary gland plays a role in medical science over blood or serum samples. Collection of saliva is simple, economical and requires minimal involvement of medical personnel. Based on the several studies, a number of biomarkers have been detected in saliva for T2DM. Patients with Type 2 diabetes mellitus are known to have a compromised salivary function as the patients are more prone to dyslipidaemia which further leads to cardiovascular diseases. Type 2 DM influences on lipid of patients which is associated with increased Cardio Vascular Disease (CVD) risk. Therefore, lipid profile analysis is a must for the treatment aspect and clinical reviews in type 2 diabetes. This review indicates the comparison between salivary and serum lipid profile in type 2 diabetics.

Keywords: Type 2 Diabetes Mellitus, Saliva, Serum, Lipid profile

INTRODUCTION

Diabetes Mellitus is characterized by insulin deficiency, cellular resistance to insulin action, or both, resulting in high blood sugar level called hyperglycaemia. It is a group of chronic diseases with related metabolic disorder. Diabetes causes various complications to our organ system mainly the eyes, kidneys and heart.

Type 2 diabetes mellitus or Non-insulin-dependent diabetes develops slowly and in a stepwise order with a group of diseases. Initially it begins with insulin resistance, which increases gradually until the body fails to maintain glucose homeostasis resulting in glucose intolerance with a variety of changes in biochemical processes [1]. Type 2 diabetes can be treated but due to its long term complications, it causes many risks to health. Prolonged high sugar level in T2DM can affect the immune, cardiovascular, renal and ophthalmic systems, leading to complications like neuropathy, peripheral vascular disease, renal disease, retinopathy and coronary heart disease. It also affects salivary glands directly [2]. Diabetic patients are highly prevalent to cardiovascular disease [3].

The group of tests which includes total cholesterol (TC), triglycerides (TGL), high-density lipoprotein-cholesterol (HDLC), low-density lipoprotein-cholesterol (LDLC) and very low-density lipoprotein-cholesterol (VLDLC) are done in serum. Similar biochemical tests can be done with other biological fluids mainly saliva because lipids are secreted in saliva. Therefore, saliva can be used for the assessment of lipid profile [4]. Lipids are influenced by the patients with type 2 diabetes thus revealing them to potential associated cardiovascular disease along with increased levels of TG, decreased levels of HDL with either normal or increased levels of LDL. This indicates that Type 2 DM influences on lipid of patients which is associated with increased Cardio Vascular Disease (CVD) risk. Hence analysis of Lipid Profile must be made an integral part in the treatment of Type 2 DM [5].

The biological fluid with numerous functions within the oral cavity, mainly facilitating the maintenance of oral health and creating the suitable ecological balance in the mouth is saliva. Human saliva mirrors the body’s health and approximately 20-30% of proteins found in human blood are also present in human saliva, highlighting the diagnostic potential of the saliva [6].

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The benefits of saliva as a diagnostic body fluid compared to blood are,

- Sampling of saliva is easy, fast, non-invasive, and allows multiple sample collections.
- The collection of saliva is very simple, reliable and painless and ideal for population based screening programs.
- The collection of saliva does not require a skilled person hence reduces the costs associated with sampling.
- The person who collects sample is away from infectious agents, such as Hepatitis and or HIV, while handling saliva [7].

The major salivary glands mainly parotid, submandibular, sub lingual and numerous minor salivary glands produces saliva. Many salivary proteins are present in saliva and can be used as good biological markers for diagnosing and detecting the progression of various diseases, as well as monitoring the effects of medicine. There are many commercially available saliva collection devices available to collect the stimulated, unstimulated or resting saliva. Stimulated saliva is collected via acid stimulation or mechanical stimulation [7]. Around 750 ml of fluid is produced per day by salivary glands in the mouth cavity. After secretion, the fluid is mixed with bronchial secretion, bacteria, nasal secretion and lining cells and is termed as whole saliva [8].

The saliva production is largely produced by the submandibular gland when a person is in a resting stage, and 20% and 8% are produced by parotid and sub lingual glands, respectively. In contrast, the saliva production is primarily derived from the parotid gland when the saliva is stimulated either via chewing gum or plastic (e.g. parafilm), or through acid stimulation. The composition of both unstimulated and stimulated saliva may be altered by physiological, environmental, pathological and genetic predisposition factors. All these factors may be responsible for the accurate derivation of results. Most of the salivary proteins are either synthesized in situ in the salivary glands or transported from blood capillaries into saliva by ultra-filtration, diffusion, or active transport. The proteins in saliva may also undergo modifications like phosphorylation, de-glycosylation and glycosylation because of different pathological conditions or as a result of exposure to many drugs and other solutions or compounds [7]. Saliva can be of two types - gland-specific saliva and whole saliva. Gland-specific saliva which can be collected directly from individual salivary glands mainly, parotid, submandibular, sublingual, and minor salivary glands. The mixture of oral fluids and other secretions from both the major and minor salivary glands, constituents of non-salivary origin, such as expectorated bronchial and nasal secretions, gingival crevicular fluid (GCF), bacteria and bacterial products, serum and blood derivatives from oral wounds, viruses and fungi, desquamated epithelial cells, food debris, and other cellular components, is the whole saliva or mixed saliva. Saliva can be collected by two methods; with or without stimulation. Unstimulated saliva is collected without exogenous gustatory, masticatory, or mechanical stimulation whereas stimulated saliva is collected by gustatory stimulation *i.e.*, application of citric acid on the subject's tongue or by masticatory action *i.e.*, from a subject chewing on paraffin. Whole saliva can be collected by spitting and draining method. In dripping method, saliva is allowed to drip off the lower lip, and in the spitting method, the subject expectorates the saliva into a test tube [9].

Constituents of whole saliva [9]:

**Salivary glands**
- Water
- Proteins
- Electrolytes
- Small organic molecules

**Microbiota**
- Oral bacteria (enzymes and bacterial products)
- Viruses
- Fungi

**Lining cells**
- Epithelial keratins

**Others Fluids**
- Bronchial and nasal secretions

**Blood and blood derivatives**
- Intraoral bleeding (serum and Cells)
- Gingival crevicular fluid (GCF: serum exudate and inflammatory cells)

**Extrinsic substances**
- Food debris
- Toothpaste and mouthrinse components

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Saritha & Manjula Shantaram “A Review on Saliva and Serum Lipid Profile levels in Type 2 Diabetics”
Saliva can be a sample of choice for diagnostic and treatment purposes but requires further investigation to find the biomolecules present in saliva during a normal healthy physiological state, as opposed to a pathological condition. For the diagnosis, prognosis, and follow up of patients with various diseases saliva can be used as a clinically informative, biological fluid. Saliva is ideal for detection of different diseases as it contains specific soluble biomarkers and it also contains variable amount of blood/serum products [7].

The figure 1 shows the presence of wide spectrum of molecules in saliva which provides valuable information for clinical diagnostic applications. For the diagnosis of systemic diseases, whole saliva is used because it contains most of the serum constituents and can be easily collected. Figure 2 shows the different systemic diseases which can be detected in saliva [10].

![Salivary Functions and clinical utility](image1)

**Figure 1.** Salivary Functions and clinical utility [10]

![Diagnosis of different systemic diseases in Saliva](image2)

**Figure 2.** Diagnosis of different systemic diseases in Saliva. [10]
The measurable and quantifiable biological parameters are the biomarkers, which can be used as indicators for health and physiology-related diagnosis, such as, environmental exposure, disease diagnosis and prognosis or pharmacologic reactions and pathogenic processes to a therapeutic modification. In the detection and diagnosis of systemic disease and oral health by using nanotechnology and molecular diagnostics, saliva plays an important, dynamic role [11]. For the identification of type 2 diabetes, a number of salivary biomarkers are detected. Salivary biomarkers are sentinel molecules whether produced by healthy individuals or by individuals affected by specific diseases that could be used to examine the health carefully and to suspect the disease. The discoveries of salivary diagnostic technologies and salivary biomarkers have been used for clinical applications. More sophisticated analytic techniques give hopefulness that saliva can ultimately be identified as a biotube for clinical diagnosis. The salivary composition and function is influenced by diabetes. The salivary functions in poorly controlled type 2 diabetes are compromised by multiple physiological factors. Salivary hypo function and dehydration in diabetes is caused by diabetes – associated autonomic neuropathies, micro vascular changes, hormonal imbalances or combination of all these complications [2].

In the human body, lipids are important for the pathological and physiological processes. In our health and disease condition, laboratory diagnosis of lipid profile is very important. Many organic compounds, mainly lipids, carbohydrates and proteins are present in saliva. Some of the studies reported the important information about salivary organic products, but least information is described about lipid components. Among numerous studies on saliva, some of the works related to the salivary lipid profile fraction and the information are often incomplete. Malgorzata et al., in their review on salivary lipids reported literature from the beginning of the study until the current state. This review shows the diagnostic use of lipids, its correlation with systemic diseases, and information about the concentrations and types of lipids in saliva in physiological and pathological condition [12]. The results based on their literature survey reported that lipids present in the saliva are important elements. Increased serum lipid concentration increases salivary lipid level. In the course of certain systemic disease saliva undergoes to change in their constituents. In the diagnosis of certain diseases, changes in the salivary lipid profile helps to find out the fluctuations in the body non-invasively [12].

The whole saliva contains 2-3 μg/ml of total lipid which consisted of triglycerides, fatty acids and cholesterol. Some researcher believed that salivary lipids are diffused directly from serum and they are glandular in origin. The role and diffusion of salivary lipids in oral health have probably not studied. Therefore, the concentrations of serum and salivary cholesterol were analysed in oral health. Karjalainen et al., assessed the salivary cholesterol in healthy adults and they concluded that serum concentration is reflected by salivary concentration levels to some extent [13]. For the premature mineralization of the dental plaque, salivary lipids play a major role in calculus formation. Hence mouth plays an important role in monitoring the systemic disease and oral health. For the evaluation of systemic disorders whole saliva is used for the salivary analysis [14]. Lipids present in saliva do not float like blood plasma lipoproteins. Therefore, their aggregation state is different from lipids in blood or lymph. Lipase activity of plasma lipoproteins was not found in parotid or submandibular saliva. The free fatty acids and partial glycerides level was high in saliva [15].

**BIOCHEMICAL ANALYSIS OF BLOOD AND SALIVA**

Sample Collection: The samples of saliva and serum are collected in the morning after overnight fast, during which subjects are advised not to drink fluids, except water or chew gum. By standardised spitting technique, unstimulated whole saliva is collected for 5 to 10 minutes between 9 to 11 am. Before collecting the saliva the subjects should rinse their mouth with water to remove any food debris, after that the subjects are seated and, after a few minutes relaxation, they are trained to avoid swallowing saliva and asked to lean forward and spit all the saliva they produced into a sterile tube or container. For the analysis of fasting blood glucose and lipid profile venous blood samples are drawn from the patient. Saliva and serum samples are centrifuged at 3000 rpm for 15 minutes. The supernatant is aspirated and stored at ~20°C until analysed [1].

Laboratory investigations include,

Fasting glucose level is determined by glucose oxidase peroxidise (GOD-POD) method [16, 17]. In this method, initial enzyme glucose oxidase (GOD) does the oxidation of glucose. 4 aminoantipyrine and phenol by hydrogen peroxide under the catalytic action of enzyme peroxidase (POD) produces quinone, the colorimetric indicator. This overall reaction is Trinder’s reaction [18]. Blood and salivary
Saritha & Manjula Shantaram “A Review on Saliva and Serum Lipid Profile levels in Type 2 Diabetics”

glucose levels correlation was found to be excellent between the study groups with 80.2816 % cases of group controlled DM showing the correlation (r value = 0.896) and 74.1321 % cases of uncontrolled DM showing the correlation (r value = 0.861) as in Table 1 [18].

Table1. Study and control groups showing the correlation between blood and salivary glucose level [18].

<table>
<thead>
<tr>
<th>Group</th>
<th>R value</th>
<th>P value</th>
<th>Interpretation</th>
<th>R square</th>
<th>Interpretation of r square value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0.678</td>
<td>&lt;0.001</td>
<td>Good correlation</td>
<td>0.459684</td>
<td>45.9684 % Cases show correlation</td>
</tr>
<tr>
<td>Controlled DM</td>
<td>0.896</td>
<td>&lt;0.001</td>
<td>Excellent correlation</td>
<td>0.802816</td>
<td>80.2816 % Cases show correlation</td>
</tr>
<tr>
<td>Uncontrolled DM</td>
<td>0.861</td>
<td>&lt;0.001</td>
<td>Excellent correlation</td>
<td>0.741321</td>
<td>74.1321 % Cases show correlation</td>
</tr>
</tbody>
</table>

(*DM: Diabetes Mellitus, R: Pearson Correlation)

Parameters of Fasting lipid profile are - Total Cholesterol (TC), Triglycerides (TG), Low Density Lipid (LDL), High Density Lipid (HDL) and Very Low Density Lipid (VLDL). Enzymatic methods are used to measure the concentration of some components of lipid profile mainly Total Cholesterol, Triglycerides, and High Density Lipid in patient’s serum and saliva. Concentration of Low Density Lipid is measured by calculating the concentration of, Total Cholesterol, Triglycerides, and High Density Lipid and the method is called Friedwald and Levy method [1]. Simranjit et al., in their studies have shown that the different values observed for each of the five parameters identified as a component of lipid profile are depicted in the shown table. The different values shown are minimum values, the maximum values, the average values and the lower and upper limits for 95% confidence interval (CI) [4].

Table2. Five parameters identified as a component of lipid profile [4].

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean±SD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total cholesterol</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum</td>
<td>111.00</td>
<td>276.00</td>
<td>198.33±43.91</td>
<td>191.40–205.26</td>
</tr>
<tr>
<td>Saliva</td>
<td>0.50</td>
<td>12.20</td>
<td>4.64±2.46</td>
<td>4.15–5.13</td>
</tr>
<tr>
<td><strong>Triglycerides</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum</td>
<td>31.00</td>
<td>194.00</td>
<td>91.14±37.26</td>
<td>84.08–98.86</td>
</tr>
<tr>
<td>Saliva</td>
<td>0.00</td>
<td>9.80</td>
<td>3.78±2.27</td>
<td>3.33–4.23</td>
</tr>
<tr>
<td><strong>High-density lipoprotein</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum</td>
<td>20.20</td>
<td>98.40</td>
<td>44.62±17.09</td>
<td>41.23–48.01</td>
</tr>
<tr>
<td>Saliva</td>
<td>0.40</td>
<td>9.24</td>
<td>2.09±1.44</td>
<td>1.81–2.38</td>
</tr>
<tr>
<td><strong>Low-density lipoprotein</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum</td>
<td>74.20</td>
<td>197.40</td>
<td>135.97±26.75</td>
<td>130.66–141.27</td>
</tr>
<tr>
<td>Saliva</td>
<td>0.12</td>
<td>8.92</td>
<td>1.97±1.76</td>
<td>1.62–2.31</td>
</tr>
<tr>
<td><strong>Very low-density lipoprotein</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum</td>
<td>6.20</td>
<td>38.80</td>
<td>18.29±7.48</td>
<td>16.81–19.78</td>
</tr>
<tr>
<td>Saliva</td>
<td>0.00</td>
<td>3.74</td>
<td>0.77±0.54</td>
<td>0.67–0.88</td>
</tr>
</tbody>
</table>

SD: Standard deviation; CI: Confidence interval

SALIVA AS A DIAGNOSTIC FLUID

Srinivasan et al., have identified specific salivary biomarkers for type 2 diabetes mellitus. They have measured more than 60% of serum proteins in saliva of type 2 diabetic patients. It has been reported nearly 50% of these proteins in saliva of diabetics. Their conclusion is that saliva can be used to measure the serum proteins in T2DM in high percentage and offers economical and attractive strategy for the screening of T2DM [19]. Ratnayake et al., have investigated certain salivary biomarkers for the detection of common systemic diseases [20].

Prathibha, et al., have studied the possible association between diabetes and salivary dysfunction. They investigated some of the salivary parameters in diabetics and non-diabetics. They concluded that there are significant variations between diabetics and non-diabetics in their salivary biochemical parameters. When compared to the blood, salivary parameters can be cost effective and a non-invasive alternative for screening, diagnosis and monitoring of diabetes [2]. Shirzaiy et al., have evaluated
some elements in saliva of diabetic patients. The findings showed that there were some alterations in salivary elements in diabetic patients even in well-controlled subjects compared to healthy group and concentrations of some salivary elements may vary in diabetic and healthy subjects based on the sex [21]. Carda et al., have compared the biochemical findings in the saliva and correlated these biochemical disturbances with the morphologic findings. They suggest that the biochemical disorders in the saliva of the T2DM patients would be related with the structural changes [22].

Shanthala et al., have shown that the diagnosis of the following conditions can be done in saliva. 1. Hereditary disease 2. Autoimmune disease, 3. Malignancy, 4. Infection, 5. Monitoring of levels of hormones, 6. Monitoring of levels of drugs 7. Bone turnover marker in saliva 8. Forensic Evidence 9. Oral diseases 10. Diagnosis of Oral Disease with Relevance for Systemic disease [23]. Marchetti et al., have studied the presence of immunoreactive insulin in saliva and plasma. They concluded that Type 2 diabetic patients, obese non-diabetic subjects, as well as normal volunteers saliva contains immunoreactive insulin. They reported that plasma and salivary insulin are related after a glucose load, and that differences exist among the three groups of subjects [24]. Fabre et al., have studied the salivary insulin method and also to determine salivary insulin levels in paediatric patients according to their age. In this study, they observed that frozen samples can maintain the insulin stability [25]. Jinhua et al., demonstrated that the T2DM and non-diabetic subjects contain resistin in their saliva. The levels of resistin in saliva are significantly higher in T2DM than those of non-diabetic controls. To evaluate inflammation, obesity, and insulin resistance state in T2DM patients, resistin levels in saliva may be used as a tool [26].

Soell et al., have studied the expression of chromogranin A and its peptides at protein level in type 2 diabetic patients’ saliva and also to obtain a new non-invasive diagnostic tool for the future. They concluded that chromogranin A, is a circulating biomarker for epithelial tumours, is also overexpressed in the saliva of type 2 diabetics [27]. Hegde et al., have studied the salivary electrolyte concentration in non-diabetic and diabetic patients with active dental caries and showed that there is a positive relationship in their salivary levels of electrolytes [28]. Venkatapathy et al., have studied the correlation between serum and salivary creatinine levels and determined the role of saliva for creatinine estimation as a non-invasive alternative to serum in patients with chronic kidney disease [29]. Hegde et al., have studied the comparison and evaluation of salivary alkaline phosphatase levels and calcium ion levels between caries active type 2 diabetics and non-diabetics. They concluded that diabetic patients have higher levels of alkaline phosphatase activity in saliva than that of non-diabetic individuals and salivary calcium ions were higher in non-diabetic individuals than diabetics [30].

Lee et al., have in their study explored non-invasive detection of T2DM by salivary transcriptomic diagnostics. By comparing microarray profiles of salivary transcriptomes, they discovered salivary mRNA biomarkers. Combination of four identified biomarkers KRAS, SAT1, EGFR, and PSMB2 were showed in their logistic regression model which could significantly distinguish T2DM patients from the healthy controls. Finally they concluded that detection of T2DM with high sensitivity and specificity, is possible in saliva by detecting RNA which could serve as a good biomarker and offer a feasible means for early detection of T2DM.[31]. Radhika et al., have in their study showed the comparison between diabetics and non-diabetics in their salivary flow rate and prevalence of subjective symptoms of xerostomia (dryness of mouth). They concluded that prevalence of xerostomia and reduced salivary flow rate is higher in Type 2 diabetics compared to non-diabetics. Alterations in salivary flow rate in type 2 diabetics create an imbalance in the homeostasis of oral environment leading to spectrum of oral problems [32]. Vaziri et al., have suggested that the determination of salivary components, specifically albumin level is useful in diabetic patients to understand their oral findings. They concluded that concentration of salivary albumin is higher in adults with T2DM and helpful in the diagnosis of oral findings in diabetics [33]. Esser et al., have determined protein composition stability of saliva. By using Surface Enhanced Laser Desorption/Ionization (SELDI) analyser they examined the protein stability at room temperature by incubating fresh whole saliva with and without inhibitors of proteases and bacterial metabolism. They determined the protein composition by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and fractionation of salivary proteins by liquid chromatography tandem mass spectrometry (LC-MS/MS). Their results showed the degradation of proteins within 30 minutes after sample collection as degradation starts during collection. Inhibitors of bacterial metabolism do not affect degradation whereas inhibitors of protease partly prevent degradation. They detected three stable degradation products of 2937 Da, 3370 Da and 4132 Da and which can be used to monitor sample quality as good markers. They identified 83 new salivary proteins. They concluded that saliva
Saritha & Manjula Shantaram “A Review on Saliva and Serum Lipid Profile levels in Type 2 Diabetics”
can be used as a diagnostic fluid in the detection of proteins [34]. Rao et al., have characterized the human salivary proteome to identify the biomarker potential to type-2 diabetes. By using multidimensional liquid chromatography/tandem mass spectrometry (2D-LC-MS/MS) they characterized type-2 diabetic and control individuals. They identified differentially abundant protein biomarkers by Label-free quantification. By Western immunoblotting and ELISA technique they independently validated selected potential biomarkers from the whole saliva of control, diabetic and pre-diabetic subjects. They identified a total of 487 unique proteins by the characterization of the salivary proteome. They concluded that type-2 diabetes can be detected and monitored by proteomic analysis of the human salivary proteome [35].

Samreen et al., have estimated the levels of specific protein biomarkers to type 2 diabetes mellitus. By using 2D liquid chromatographic system they analysed plasma proteins. Initially by chromatofocusing they fractionated the sample and the selected fractions were further analysed by reverse-phase high performance liquid chromatography. MALDI-TOF analyser was used to identify the proteins which showed variation between control and test sample. The samples were then analysed by ELISA and four proteins were estimated which were found to vary. They found to decreased levels of Apo lipoprotein A-I by −6.4% and increased level of Apo lipoprotein E, leptin and C reactive protein (CRP) by +802, +842 and +872%, respectively, in the diabetic patients. According to their study, discovery of these marker proteins might provide an adjunctive method for early detection of risk for diabetes [36]. Dodds et al., have determined the alteration in type 2 diabetes mellitus with a healthy, non-medicated control group, and also a group of hypertensives in their saliva output and composition. Their conclusion was that decreased flow rates and increased protein concentrations of saliva were similar in all the groups but consistently greater in diabetics than the hypertensive. According to their study they suggest that diabetics may be more prone to oral dryness and infections than non-diabetics [37].

Glucose Level in Blood and Saliva

Panda et al., have, in their study, to diagnose and monitor diabetes found a medium, which could play a major role in diagnostic field. To verify the role of saliva as a diagnostic tool, they compared saliva samples with blood and determined glucose and glycated haemoglobin level in diabetic and non-diabetic healthy subjects. According to their findings there is a highly significant correlation coefficient between serum glucose level and salivary glucose level, as well as between HbA1c percentage and salivary glucose level [38]. Panchbhai et al., have in their study assessed salivary flow rate in diabetics and healthy non-diabetics and evaluated saliva samples for glucose, amylase and total protein levels. By using these parameters they also analysed duration and type of diabetes mellitus and identified the interrelationships among the variables included in the study [39]. Balan et al., have done a comparative analysis of the salivary concentrations. Based on their study they reported that diabetics have higher concentration of glucose in their saliva but it is not influenced by hyperglycaemia[18].

Jurysta et al., have studied the revaluation of glucose concentration and excretion in mechanically stimulated and unstimulated saliva in diabetic and normal non diabetic subjects. There is a decreased salivary glucose concentration, increased salivary flow, and unchanged glucose excretion rate was recorded in normal non diabetic subjects while comparing unstimulated saliva to stimulated saliva. But in diabetic patients, salivary glucose concentration and excretion rate were unchanged and an increase in salivary flow rate was observed under the same experimental conditions. They reported that diabetic patient’s saliva has higher glucose concentration and excretion than in control subjects, whether in stimulated or unstimulated saliva. They found that there is no significant correlation between glycaemia and either glucose concentration or glucose excretion rate in the diabetic patients, whether in stimulated or unstimulated saliva. They also compared diabetic patients to control subjects, and they found the relative increase in concentration of salivary glucose was comparable to that of concentration of blood glucose. They also documented various relationships between normal subjects and diabetic patients by doing an oral glucose tolerance test [40].

Singh et al., have detected glucose level in saliva and plasma of diabetic and non-diabetic subjects and compared concentration of glucose. They concluded that salivary glucose may be the potential marker in the detection of diabetes. This study confirmed that controlled and uncontrolled diabetics have high concentration of glucose in their saliva and plasma [17]. Vasconcelos et al in their study, comparatively evaluated the concentrations of saliva and blood glucose as well as xerostomia and
salivary glucose in type 2 diabetic and non-diabetic patients. They concluded that concentration of salivary glucose was significantly high in the experimental group and they also found that there was no correlation between blood and salivary glucose concentrations in diabetic patients. They reported that in diabetic patients the total salivary flow was significantly reduced and there were no significant difference as to the presence of xerostomia in type 2 diabetic and non-diabetic patients [41]. Shukira et al., have in their study evaluated the saliva samples for levels of salivary total protein, salivary glucose, alpha amylase, and of salivary flow rate in type 2 diabetics and non-diabetic subjects in both genders. They concluded that type 2 diabetic patients have lower value of salivary amylase and salivary flow rate and higher concentration of salivary glucose. They found that there was no significant difference seen in protein value in all groups [42]. Iyanoyski et al., have in their study determined the degree of severity of xerostomia, salivary concentrations of urea and glucose in patients with type 1 diabetes or insulin-dependent diabetes, and they also determined the correlation between salivary glucose levels and xerostomia. They concluded that xerostomia is caused by diabetes and they also found that there is a significant correlation between the salivary levels of glucose and degree of xerostomia in type one diabetics [43].

Lipid Profile in Serum and Saliva

Singh et al., have in their study, evaluated the comparison between the salivary and serum lipid profile levels in healthy subjects and to corroborate the function of saliva as a non-invasive diagnostic medium for the estimation of lipid profile[17]. Jain et al., have planned to assess the comparison between lipid profile and HbA1c level. According to their study, in the prediction of lipid profile in diabetics, HbA1c level can be used as the best indicator. So, in the screening of diabetic patients in association with CVD, HbA1c test is helpful [44].

Samatha et al., have conducted a study between diabetic patients and healthy controls to compare the level of lipid profile. They concluded that diabetic patients had elevated levels of total cholesterol, triglycerides and low density lipids. This indicates that dyslipidaemia, is more common in diabetic patients, and may cause cardiovascular disorders [16]. Rajeshwari et al., have analysed the correlation between high density lipid and low density lipids in plasma with MDA and total thiols in diabetic patient’s saliva. They concluded that results acquired by the correlation between plasma lipid profiles with the salivary markers of oxidative stress show the ability of saliva as a non-invasive diagnostic tool in the diagnosis and prognosis of diabetes. This indicates that saliva can be used as a choice of sample in the detection and treatment of different pathological diseases [45]. Daniel and Philip have determined the effect of lipid profile on type 2 diabetes mellitus. Patients with type 2 diabetes influences lipids, thus disclosing them to cardiovascular disease. They concluded that patients with type 2 diabetes mellitus had increased levels of triglycerides, decreased levels of high density lipid with either normal or increased levels of low density lipid. This indicates that type 2 diabetes influences on patients abnormal lipid profile along with increased risk of cardiovascular disease. Thus analysis of lipid profile in type 2 diabetics is very important in the clinical reviews and treatment [5]. Popa et al., have studied that all the subjects with type 2 diabetes are at a higher risk of cardiovascular disease (CVD). Their Current interest is in identification and development of novel biomarkers which are specifically designed for individuals with diabetes [46].

CONCLUSION

Based on the results of several studies on salivary biomarkers, it is found that saliva can be used as a non-invasive medium in the identification and determination of glucose and lipid profile levels in type 2 diabetic patients. These studies are based on the results of age, sex, history, lifestyle and study sample sizes. Hence, there are many unknown salivary biomarkers which may also have used to determine the diagnostic quality of saliva, instead of blood in type 2 diabetic patients. Consequently, future studies with larger sample size, new methodologies and identification of different salivary biomarkers may lead to the better understanding of saliva as a choice of sample for various diseases.

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