European Journal of Molecular & Clinical Medicine
ISSN 2515-8260 Volume 07, Issue 01, 2020

SALIVA IN DIABETES-A REVIEW

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ABSTRACT

Saliva is a unique fluid which plays an important role in maintaining the normal oral health of an individual. Diabetes is the major factor that leads to the changes in the salivary pH, salivary flow and dental caries. 32 articles were collected from the pubmed website and were included as citations in our present review. Salivary glucose and blood glucose level are directly proportional to each other. Normal level of salivary glucose is 0.5-1.00 mg/ml. Salivary hypofunction in diabetic individuals is observed. Diabetes leads to the reduction of salivary pPH and salivary flow. It also helps in multiplication of harmful microorganisms in the oral cavity.

KEY WORDS: Diabetes, Glucose concentration, Salivary composition, Salivary flow, Salivary total protein,

INTRODUCTION

Saliva is a viscous solution which has both organic and inorganic constituents. Saliva plays a leading role in maintaining oral health, it helps to construct and maintain the health of soft and hard tissues, when the salivary flow is reduced it may cause oral health problems such as dental caries and other bacterial infections. Saliva is an exocrine solution constituting 99% water and the remaining 1% constitutes proteins and electrolytes. Saliva is secreted from 3 major and 4 minor salivary glands they are as follows : submandibular gland (constitutes around 65%), parotid gland (constitutes around 20%), sublingual gland (constitutes around 5 to 7%) major salivary glands. Labial, lingual, buccal and palatine salivary gland all together (constitutes lesser than 10%) minor salivary gland. The major functions of saliva are, providing lubrication and maintaining tooth integrity (Dodds *et al.*, 2015). Saliva is also used as a diagnostic tool for salivary gland disorders and oral squamous cell carcinoma (Hema Shree *et al.*, 2019). Age is considered as a very important tool to diagnose any disease, so the most common method used to estimate an individual's age is by Olze's method (Palati *et al.*, 2019). According to many studies done, it is found out that older people are the ones who are more prone to oral disease like xerostomia (Palati *et al.*, 2020). But physicians compassion and empathy have been correlated with improved control of chronic diseases such as diabetes and rheumatoid arthritis. All of this is only possible due to the usage of modern instruments (Prasanna and Gheena, 2016), (Ahad and Gheena, 2016).

Diabetic patients usually have higher concentration of glucose, calcium and urea,which leads to several oral diseases, like xerostomia and oral lesions. Diabetic patients have more salivary glucose compared to normal individuals. The total amylase concentration is considered to be lower in diabetic patients. Diabetic patients are considered to have a very high IgA antibody concentration compared to normal individuals. Early stage of diabetes can be detected by the presence of IgA insulin in saliva (Lima-Aragão *et al.*, 2016). Photography plays an important role in forensics. It helps us to keep a record on all the clinical

observations that are observed during a case (Hannah et al., 2018). Saliva is often detected in crime scenes along with bite marks or lip prints where the oral cavity may have been involved (Abitha and Santhanam, 2019)(Harrita and Santhanam, 2019). Such cases can be misled due to medical negligence (Uma *et al.*, 2020). This may lead to physical and mental problems in affected individuals (Krishnan *et al.*, 2018). Climatic change is also said to play a major role in human health due to invasion of microbes (Sarbeen and Gheena, 2016). The main aim of this review is to spread knowledge about the changes in pH, salivary flow, dental caries and salivary composition due to diabetes.

METHODOLOGY

This research was conceived as a scoping literature review. First, we sought existing reviews in the last 2 decades that had assessed the evidence for (saliva in diabetes) using a structured approach. We did not follow a systematic review protocol as the research field is still not sufficiently populated to accommodate systematic reviews or meta-analysis in seeking to identify relevant literature from the last 30 years, we accessed databases that are commonly used to index health and medical research, including Pubmed, Google scholar and CrossRef. Searches of the reference lists from relevant review articles were also employed to identify further relevant studies. Search terms include (salivary composition), (change in pH and salivary flow due to Diabetes), (role of insulin in saliva). The manuscript was rewritten in english. Searches of the England-language literature were prioritised to ensure the accessibility of reviewed manuscripts for an international readership.The level of evidence of the reviewed articles were categorized as per the criteria of Centre for Evidence-Based Medicine, Oxford, and UK (Howick, 2011).

Salivary composition on diabetic patients

In diabetic patients salivary composition is altered. Glucose concentration was significantly higher in saliva of Insulin-Dependent Diabetes Mellitus (IDDM) patients. Potassium concentration was significantly higher in both resting and stimulated saliva. There were no significant changes between diabetics and healthy individuals in sodium and IgA concentration (or) in amylase activity. All these changes in the salivary composition leads to dry mouth in IDDM patients (Ben-Aryeh *et al.*, 1988)**.**

Changes in salivary total protein due to diabetes

There were no significant changes observed in the mean values of total protein count between Insulin Dependent Diabetes Mellitus patients (6.65 + or - 0.84 g/dl) and healthy individuals [(6.35 + or - 0.76 g/dl) (Ladgotra *et al.*, 2016)]. The mean salivary total protein count in diabetic patients was significantly lowered (91.80 + or - 6.61 mg/dl) when compared to healthy individuals [(103.10 + or - 5.46 mg/dl) (Indira *et al.*, 2015)].

Changes in pH due to diabetes

Diabetes causes the body's pH levels to become more acidic which leads to a condition known as ketoacidosis. The salivary pH was significantly lowered in diabetes patients when compared to normal individuals [(ND=7.09 + or - 0.29, D= 6.69 + or - 0.35, $p<0.0001$) (KM *et al.*, 2013)] where as the study done by Seethalakshmi states that the salivary pH was 6.51 in the study group (diabetes patients) and 7.88 in the control group [(non diabetic patients) (Seethalakshmi *et al.*, 2016)]. Many authors have identified a PH of 3.8 to 5.2 in patients with diabetes and periodontitis (Tn and P, 2016)..

Changes in salivary flow due to diabetes

The normal saliva production varies between 0.5 to 1.5 liters. The unstimulated salivary flow rate varies between 0.3 - 0.4 ml/min. This rate reduces to 0.1 ml/min during night and increases to 0.5 ml/min in day time. Salivary flow rate in type 1 diabetes was (0.35 + or - 0.11 ml/min) lower than control group 1 (0.50 + or - 0.07 ml/min). The same difference was observed between type-2 diabetes (0.37 + or - 0.13 ml/min) and control group 2 (0.47 + or - 0.11 ml/min) (P=0.01). No significant difference was observed between

type 1 and type 2 diabetics (Hoseini *et al.*, 2017). The salivary flow rate of type-2 diabetic patients was found to be 2.17 + or - 0.91 ml/min and in healthy individuals it was found to be 2.93 + or - 1.29 ml/min. This study was done on stimulated saliva (Srivastava *et al.*, 2018). The salivary flow rate ranged between 0.05 and 2.1 ml/min, with a mean value of 0.52 + or - 0.42 ml/min (Lima *et al.*, 2017)**.**

Effect of dental caries due to diabetes

Dental caries increases in diabetic patients compared to non diabetic individuals.10.66 is the average value for diabetic individuals whereas 5.6 is the average value for normal people (Latti *et al.*, 2018). The mean DMFT index was higher in the diabetic individuals (8.10) when compared to that of non diabetic participants (Seethalakshmi *et al.*, 2016).

Effect of diabetes in saliva

Type-1 diabetes is most commonly seen in children. It is caused due to chronic hypoglycemia and disturbance in the metabolism of carbohydrates, fats and proteins. Children with type-1 diabetes have increased activity of N-acetyl -beta-D-hexosaminidase due to increased catabolism of glycoconjugates (Zalewska-Szajda *et al.*, 2013).

Relation between blood glucose and sSalivary glucose

There is a positive relationship between salivary and serum glucose in diabetic patients. Hence, salivary glucose was found to be an indication of serum glucose concentration in diabetic patients. HbA_1C levels in diabetic patients also have a positive relationship with salivary glucose level (Abikshyeet *et al.*, 2012). The average salivary glucose value in diabetic patients was found to be 8.47 mg/dl with a SD of 4.20 whereas in healthy individuals, the mean salivary glucose level was found to be 1.20 mg/dl with a SD of 0.86. Blood glucose level in controls was R= 0.6342 and blood glucose level in diabetes was R=0.8809 (Dhanya and Hegde, 2016).

Management of hyposalivation in diabetes

Individuals with type 2 diabetes with hyposalivation can be treated by giving immunologically active saliva substitutes which helps them to reduce the amount of plaque, gingivitis and positive yeast counts (Montaldo *et al.*, 2010). Hyposalivation and oral lesion is considered as a symptom of Mucoepidermoid carcinoma. In order to diagnose these symptoms, biopsy of parotid salivary gland has to be done (Sheriff and Santhanam, 2018).

DISCUSSION

Salivary glucose and blood glucose level are directly proportional to each other . The normal level of salivary glucose is 0.5-1.00 mg/100 ml. It is stated that salivary glucose is closely related to the oral environment in patients with diabetes. But researchers have found that salivary glucose does not have any effect on oral health or support the growth of microorganisms (Shreya Gupta *et al.*, 2017)(Gupta *et al.*, 2017). Bhagyashri *et al* states that, with increase in age, blood glucose level, DMFT values and dental caries increases in diabetic patients . Salivary secretion also reduces in diabetic patients due to alteration of salivary composition (Ben Aryeh *et al.*, 1988). The pH of saliva gets reduced in diabetic patients. This happens due to metabolic changes which results in acidic pH. The most common genetic problems that are observed in oral cavity are gingival pigmentation and tooth sensitivity (Manohar and Abilasha, 2019), (Gunasekaran and Abilasha, 2016). Molar incisor hypomineralization is an endemic pediatric disease which is very much related to saliva and it's protein composition (Padavala and Sukumaran, 2018).

CONCLUSION

Off late there have been many researchers conducted to understand the correlation between saliva and diabetes. Diabetes causes many changes in the salivary composition and also leads to the decrease in salivary flow and pH.

CONFLICT OF INTEREST.

None declared.

AUTHOR CONTRIBUTIONS

Danisca Uthayasankar:literature research ,data collection, analysis,manuscript writing. Gifrina Jayaraj :Data verification ,manuscript drafting, R Gayathri : Data verification, manuscript drafting.

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Table 1: Description of included studies

S.No	Author	Year	Study	Quality analysis	Population	Sample	Inference
1.	Padmavathi BN (Srivastava *et al.*, 2018)	2018	A case control study	Level 3	Indian population	30 Type 2 DM patients	Salivary flow rate in type 2 diabetes patients was 2.17 + or - 0.91 ml/min and in healthy individuals the salivary flow was 2.93 + or - 1.29 ml/min. This study was done on stimulated saliva
2.	Latti BR (Latti *et al.*, 2018)	2018	A Case control study	Level 3	Indian population	30 DM patients	Dental caries increases in diabetic patients compared to non diabetic individuals.10.66 is the average value for diabetic individuals whereas 5.6 is the average value for normal people.
3.	Lima DLF (Lima *et al.*, 2017)	2017	ACross sectional clinical study	Level 2	Brazilian population	120 Type 2 DM patients	The salivary flow rate ranged between 0.05 and 2.1 ml/min, with a mean value of 0.52 + or - 0.42 ml/min
4.	Hoseini A (Hoseini *et al.*, 2017)	2017	A Case control study	Level 3	Iranian population	40 Type 1DM patients and 40 Type 2 DM patients	Salivary flow rate in type 1 diabetes was (0.35 + or - 0.11 ml/min) lower than control group 1 (0.50 + or - 0.07 ml/min).

							The same difference was observed between type 2 diabetes (0.37 + or - 0.13 ml/min) and control group 2 (0.47 + or - 0.11 ml/min) (P=0.01).No differences was observed between Type 1 and Type 2 patients in salivary flow rate
5.	Gupta S (Gupta *et al.*, 2017)	2017	Cross sectional study	Level 2	Indian population	40 controlled DM patients and 40 uncontrolled DM patients	Saliva glucose used to measure glycemic level in DM patients
6.	Lima-Aragao MVV (Lima-Aragão *et al.*, 2016)	2016	Controlled based study	Level3	Brazilian Population	88 Diabetic adults	Salivary concentration of Glucose, calcium & Urea are observed in diabetic patients.
7.	Seethalakshmi C (Seethalakshmi *et al.*, 2016)	2016	Cross sectional study	Level 2	South Indian population	20 DM patients	salivary PH was 6.51 in the study group(diabetes patients) and 7.88 in the control group(non diabetic patients).
8.	Uma Maheshwari (Tn and P, 2016)	2016	A case control study	Level 3	South Indian population	20DM patients with periodontitis	PH of 3.8 to 5.2 in patients with diabetes and periodontitis was observed
9.	Hedge S (Dhanya and Hegde, 2016)	2016	ACase control study	Level 3	Indian population	100 DM patients	The mean salivary glucose in diabetic patients was 8.47

							mg/dl with a SD of 4.20 whereas in healthy individuals, the mean salivary glucose level was 1.20 mg/dl with
10.	Amit Ladgotra (Ladgotra *et al.*, 2016)	2016	A comparitive study	Level 2	Indian population	60 DM Patients	There was no significant changes observed in the mean values of total protein count between IDDM patients (6.65 + or - 0.84 g/dl) and healthy individuals (6.35 + or - 0.76 g/dl) .
11.	Michael Dodds (Dodds *et al.*, 2015)	2015	Systemic Review	Level 4	-	-	The major functions of saliva are , providing Lubrication and maintaining tooth integrity
12.	M Indira (Indira *et al.*, 2015)	2015	A comparitive study	Level 2	Indian population	20 type 2 DM Patients	The mean salivary total protein count in diabetic patients was significantly lowered (91.80 + or - 6.61 mg/dl) when compared to control group (103.10 + or - 5.46 mg/dl)
13.	Prathiba KM (K M *et al.*, 2013)	2013	A cross sectional study	Level 2	South Indian Population	30 Type 2 DM patients	The salivary PH was significantly lowered in diabetes patients when compared to normal individuals (ND=7.09 + or - 0.29, D= 6.69 + or - 0.35, $p<0.0001$) .

14.	Zalewska-Szajda (Zalewska-Szajda *et al.*, 2013)	2013	Original research	Level 2	Poland population	65 Type 1 DM patient	Increase in the concentration and specific activity of HEX in Type 1 DM patients
15.	Abikshyeet (Abikshyeet *et al.*, 2012)	2012	Original research	Level 2	Indian population	106 Type 2 DM patients	Salivary glucose was found to be an indicator of serum glucose concentration in DM patients
16.	Montaldo L (Montaldo *et al.*, 2010)	2010	Randomised controlled trial	Level 1	Italian population	65 Type 1 DM patients	Immunologically active saliva substitutes help in reducing plaque,gingivitis and positive yeast counts.
17.	Ben-Aryeh (Ben-Aryeh *et al.*, 1988)	1988	Comparative study	Level 2	Israel population	35IDDM patients	Increase in glucose and potassium concentration in saliva