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SALIVA-THE KEY REGULATOR OF ORAL CHANGES IN DIABETES PATIENTS

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ABSTRACT: Saliva plays the most important role in the maintenance and preservation of the health of our oral cavity. In diabetes mellitus functions of salivary glands are impaired and as a consequence xerostomia develops. Hoposalivation leads to various oral mucosa alterations, ulcerations, taste alterations, burning mouth, dental decay, halitosis and various infections. All these alterations can compromise patient's quality of life. Saliva can also be used as a diagnostic tool as well as marker for monitoring diabetes mellitus.

INTRODUCTION: Diabetes mellitus can be explained as clinically and genetically heterogeneous group of disorder which is characterized by a relative or absolute insufficiency of insulin secretion and/or resistance to the metabolic action of insulin on target tissues.

This is a systemic disease affecting every system of the body. According to American Diabetes Association (2012); "Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially of eyes, kidneys, nerves, heart and blood vessels [1].

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Long standing hyperglycaemia besides damaging various systems of body may also impair salivary gland functions, which leads to a reduction in the salivary flow and changes in saliva's composition. As a consequence various dental as well as mucosal alterations can occur which include proliferation of various pathogenic microorganisms, taste alterations, burning mouth, dental caries, coated tongue and halitosis [2, 3, 4].

Classification and Pathophysiology of Diabetes Mellitus: The incidence of diabetes is increasing such alarming rate in our country that India can be called as **"**Diabetic Capital of the World" [5]. As per The report published by the International Diabetes Federation (IDF) and the Madras Diabetes Research Foundation, India had 62.4 million people with type 2 diabetes in 2011 compared with 50.8 million the previous year. The IDF predicts, India will have 100 million people with diabetes by 2030 [6]. As per recent classification system which is followed worldwide at present, four types of diabetes mellitus: type 1, type 2, "other specific types" and gestational diabetes.

"Other specific types" contains diabetes mellitus of various known etiologies.[7]

Type-1 diabetes mellitus was previously known as insulin-dependent diabetes mellitus and type 2 diabetes mellitus was as non-insulin-dependent diabetes mellitus.

Type-1 diabetes results from cell mediated autoimmune destruction of pancreatic beta cells; as a consequence there is total loss of insulin secretion.

Type-1 diabetes is commonly seen in children and adolescents but it can be seen in older people also. In older type-1 diabetes patients the beta cell destruction occurs more slowly compared to adolescents and children with less abrupt onset of symptoms. Hence exogenous insulin is necessary to sustain life of these patients. In the absence of insulin, these patients develop ketoacidosis a life threatening condition [8, 9, 10].

On the other hand Type-2 diabetes results due to insulin resistance as well as altered insulin production. Insulin resistance alters the use of endogenously produced insulin at the target cells. As in this situation autoimmune destruction of beta cells does not occur, these patients retain the capacity for some insulin production. Hence incidence of ketoacidosis is very low. In type- 2 diabetes hyperglycemia appears gradually. Early in this disease process to compensate insulin resistance insulin production is actually increased. As the condition progress; due to prolonged increase in secretory demand, pancreatic insulin production gets diminished. Gradually insulin secretion become insufficient to compensate for insulin resistance and patients develops symptoms [9, 10].

Composition and Function of Saliva: The most important function of salivary glands is production and secretion of saliva. Human saliva is made up of 99.5% water; the other 0.5% consists of electrolytes, mucous, glycoproteins, enzymes, and antibacterial substances such as secretory IgA and lysozyme. In addition to these components saliva contains desquamated oral epithelial cells, microorganisms and their products, leukocytes, gingival crevicular fluid and food remnants.

The total volume of daily salivary secretion is 750 ml, of which submandibular glands produce 60%, parotids 30%, sublinguals 5% and about 7% is contributed by minor salivary glands. The pH of whole saliva varies from 6.7-7.4 whereas saliva from parotid gland varies from 6.0-7.8 [11, 12, 13].

TABLE 1: THE MAJOR COMPONENT OF SALIVA AND THEIR FUNCTIONS ARE AS FOLLOWS [3]

FUNCTION		COMPOSITION
Protection	Lubrication, Water proofing, Lavage Pellicle formation.	Glycoprotein Water
Buffering	Maintains pH unstable for colonization Neutralizes acid	Phosphates Bicarbonates
Digestion	Bolus formation Neutralizes esophageal contents and digest starch	Phosphates Bicarbonates Amylase
Taste	Solution of molecules Taste bud growth and maturation	Water
Antimicrobial	Barrier effect Antibody	Gustin, Glycoprotein, IgA,IgG,IgM Lysozyme and lactoferrin
Tooth integrity	Hostile environment Enamel maturation and repair	Calcium, phosphate and fluoride

Alterations of Salivary Glands in Diabetes Mellitus: Sialosis can be described as a multi factorial disease of the salivary glands which is characterized by a painless bilateral growth. This growth is commonly seen in parotid gland and followed by a decreased salivary production which invariably leads to xerostomia. Other glands may also be involved.

Various literatures have described Sialosis as a specific consequence of diabetes. In diabetic sialosis, the increased volume of the glands is due to the infiltration of adipose in the parenchyma. These alterations can be found both in the acinar as well as ductal cells [4, 10, 14].

This disease is a degenerative disease caused by a desmyelinization and consequent atrophy of the mioepithelial cells and linked to an alteration in the neuro-autonomic regulation of the gland. Hence, the sialosis impair the secretory mechanism that is a result of a stimulation of alpha and beta adrenergic receptors of the acinar cells which causes exocytosis [4, 14].

On the other hand, some authors have opinionated that decrease in salivation in diabetes mellitus could be attributed to increase of diuresis or polyurea, which decreases extracellular liquid and as a consequence reduction of saliva production [4, 14]. Various studies has shown that increased incidence of decay, fissured tongue, glossodynia, ulcers, cheilitis, various infections and denture intolerance are common in diabetes mellitus patients, in which xerostomia plays the key role [15].

Taste alterations in Diabetis and Role of Saliva: Taste alteration refers to a decrease in the ability to taste foods (hypogeusia), Changes in what food normally tastes like (dysgeusia), or the complete loss of the ability to taste foods (ageusia). It also refers to the presence of a metallic or medicine-like taste in the mouth [16].

They are generally associated to the reduction of salivary flow, low production rate of gustin, zinc deficiency which leads to a decreased gustin synthesis, and coated tongue. Coated tongue is commonly produced due to accumulation of sulfide compounds which present a sour taste [4].

Various studies have reported that patients with poorly controlled diabetes may have an impaired taste response, which has a direct correlation with glucose levels and is independent of somatic or autonomic nerve function. In diabetes mellitus there is deficiency or absence of gustin. Gustin constantly maturates taste papillae [17], hence in this disorder taste alterations happen.

This abnormal taste alteration may influence the choice of nutrients, with a preference for sweet-tasting foods that exacerbate hyperglycemia. With the necessity to feel the salty taste, diabetic people frequently increase their salt intake, which leads to development of hypertension or worsen the pre-existing hypertensive state [4, 10].

Coated tongue and Halitosis in Diabetes -The Role of Saliva: Coated tongue is a bacterial mass that grows on the tongue surface with the exfoliated mucosa cells and food debris. The most frequently found bacteria of tongue coating are anaerobic Gram negative bacteria .They generally initiate its proliferation in the deepest interpapillary region where there is almost no oxygen.

In diabetes patients salivary flow rate is low as well as their high viscosity saliva causes a reduction in its cleaning capacity. Their salivary antimicrobials factors also get reduced. All these together facilitate coating of tongue.

When tongue's coat in diabetic patients gets contaminated by anaerobic proteolytic microorganisms, they produce volatile sulfide compounds; among which sulfide hydrogen is the most abundant. It gives the smell of rotten

Egg Sometimes metylmercaptan and dimetylsulfide are also produced in lower rates [4, 10]. Halitosis with a typical smell of fruit (ketonic smell) is one among the many causes of halitosis in diabetic population.

Infections in Diabetis and Role of Saliva: Fungi are microorganisms that are naturally found in the oral cavity. Patients with diabetes are more prone to develop infections; among which buccal and oropharyngeal Candidiasis is the most common. Buccal and oropharyngeal candidiasis is one of the most frequent opportunistic infections found in patients with impaired immunological resistance.

Candida albicans grows rapidly in diabetes patients as this disease impairs local immunological resistance due to reduction of salivary flow; reduction of salivary antimicrobials factors, reduced action of antimicrobial factors and higher salivary glucose concentration [18-22].

Decay in Diabetes and Role of Saliva: The association of tooth decays and diabetes is controversial.

Some studies did not find any association between the two diseases whereas other studies have shown that diabetic patients with a poor metabolic control are more prone for tooth decay. Logically, hyposalivation and change in constituent of saliva that occur in diabetic patients should be favorable for dental caries [23, 24,]

To detect protective role of salivary pH, salivary flow rate, and salivary calcium in the patients of type-2 diabetes mellitus with dental caries, Muhammad Jawed *et al* studied 400 type-2 patients of diabetes mellitus and 300 age- and sex matched controls and found; salivary pH, flow rate, and calcium levels were low in diabetics as compared to controls. They concluded that, optimum salivary calcium level might supply calcium continuously to arrest the demineralization and help reducing the dental caries occurrence [23].

Burning Mouth in Diabetis and Role of Saliva: Burning mouth syndrome is a painful, frustrating condition often described as a scalding sensation in the tongue, lips, palate, or throughout the mouth. Although it can affect anyone, but middle-aged or older women are most commonly affected.

It has been frequently reported that the burning sensation starts in the tongue and gradually spreads throughout the whole mouth. Patients may feel pain, tingle or paresthesia in the throat, lips, gingiva or palate also. Besides candidal infection, Stress and anxiety; Systemic diseases such as diabetes mellitus may also be a causal factor. Burning mouth syndrome in diabetes patients could be related to hyposalivation [4, 10, 25].

Biochemical Alterations of the Saliva in Diabetes: Biochemical alterations of the saliva found in diabetic patients are related to glucose concentration, total protein levels, albumin, lysozymes, peroxidase, electrolytes (sodium, potassium, chloride, phosphorus, magnesium and calcium), amylase, IgA and buffer capacity. These are helpful for diagnostic and purpose of disease monitoring [4].

On the other hand, it was found that biochemical findings in saliva of diabetic group differ depending upon different study population.

To substantiate the role of saliva as a diagnostic tool Abikshyeet P *et al* compared saliva samples with blood glucose and glycated hemoglobin (HbA1c) in healthy and diabetes mellitus patients and found significant correlation between them. [26]

Malathi *et al* studied 30 non-insulin dependent diabetes mellitus patients and compared them with healthy subjects to provide salivary amylase level as a bio-chemical indicator for diagnosing and monitoring the glucose levels. In their study highly significant difference in the mean scores regarding salivary amylase was found [27].

Andelski-Radicevic Biljana *et al* studied whole of unstimulated and stimulated saliva to estimate any changes in glucose, total proteins, albumin, sodium and potassium concentration in saliva of diabetes patients compared to non-diabetics and found significant changes [28].

Negarto *et al* in their extensive review mentioned about the study of Pacheco *et al* where 30 type 1 and 30 type 2 diabetic patients with good metabolic control were studied compared to 30 non-diabetic subjects to find changes that occur in the whole non-stimulated saliva flow rate and its composition. It was found in spite of good metabolic control type 1 diabetes people presented changes in the levels of phosphate and type 2 patients had changes in salivary flow and calcium concentrations [4, 29].

CONCLUSION: Saliva plays the most important role to maintain the health of oral cavity. Various oral alterations due to hyposalivation in diabetes mellitus can compromise patient's quality of life. In addition to; Saliva offers an alternative to serum as a diagnostic fluid that can be collected in a non-invasive manner by individual with minimal training.

Hence medical as well as dental professionals should receive a more expanded knowledge on pathophysiology of various changes in diabetes and their correlation with saliva to serve patient better.

REFERENCES:

1 Diagnosis and Classification of Diabetes mellitus, Position Statement, American Diabetes Association, Diabetes Care, January 2012; 35(1): S64- S71.

2 Manfredi, Mc Cullough, Vescovi, Kaarawi, Porter, Update on diabetes mellitus and related oral diseases, Oral Diseases.2004; 10: 187–200.

3 Ira B. Lamster, Evanthia Lalla, Wenche S. Borgnakke and George W. Taylor, The Relationship Between Oral Health and Diabetes Mellitus, JADA 2008;139(5):19S-24S.

4 Negrato and Tarzia, Buccal alterations in diabetes mellitus, Diabetology & Metabolic Syndrome, 2010; 2(3), 1-11.

5 V. Mohan, S. Sandeep, R. Deepa, B. Shah & C. Varghese, Epidemiology of type 2 diabetes: Indian scenario, Indian J Med Res 125, 2007; 217-230.

6 Priya shetty, India's diabetes time bomb, nature, 2012; 485:s14-s16.

7 Definition, Diagnosis and classification of Diabetes Mellitus and its complications, Report of a WHO consultation, World Health Organization-1999.

8 Al Homsi and Lukic, An Update on the pathogenesis of Diabetes Mellitus, ijod.uaeu.ac.ae/iss.

9 Ralph A. De Fronzo, Pathogenesis of type 2 diabetes mellitus, Med Clin N Am 88,2004; 787–835.

10 Manfredi, Mc Cullough, Vescovi, Kaarawi, Porter, Update on diabetes mellitus and related oral diseases, Oral Diseases,2004; 10: 187–200.

11 G S Kumar: Orban's Oral Histology & Embryology. Elsevier, 12th edition 2010

12 Antonio Nanci: Ten Cate's Oral Histology. Elsevier, 7th edition 2008.

13 Masthan K M K: Textbook of Human Oral Embryology, Anatomy, Physiology, Histology and Tooth Morphology.Jaypee Brothers Medical Publishers,1st edition 2010.

14 Carda C, Carranza M, Arriaga A, Diaz A, Peydró A, Ferraris MEG: Structural differences between alcoholic and diabetic parotid sialosis. Med Oral Patol Oral Cir Bucal 2005; 10(4):309-314.

15 Alliny de Souza Bastos, Andressa Rosa Perin Leite, Rubens Spin-Neto, Patrı´cia Oehlmeyer Nassar, Elaine Maria Sgavioli Massucato, Silvana Regina Perez Orrico, Diabetes mellitus and oral mucosa alterations:Prevalence and risk factors,Diabetes research and clinical practice, 2011;92:100-105

16 www.healthline.com/search?q1=taste+alteration&submitbtn=

17 A R Shatzman and R I Henkin, Gustin concentration changes relative to salivary zinc and taste in humans, Proc Natl Acad Sci U S A. 1981; 78(6): 3867–3871.

18 Taper-Jones, Aldred, Walker, Hayes, Candidal infections and populations of Candida albicans in mouths of diabetics, J Clin Pathol 1981; 34:706-711.

19 GA. Bartholomew, B. Rodu, and D. S. Bell, Oral Candidiasis in Patient with Diabetes Mellitus Diabetes Care, 1987; 10(5).

20 BV Kumar, NS Padshetty, KY Bai, MS Rao, Prevalence of Candida in the Oral Cavity of Diabetic Subjects, JAPI ,2005;53 :598-602.

21 Khaled H Abu-Elteen, Mawieh A Hamad, Suleiman A. Salah, Prevalence of Oral Candida Infections in Diabetic Patients, Bahrain Medical Bulletin,2006;28(1).

22 Radmila R. Obradović, Ljiljana G. Kesić, Ana N. Pejčić, Milica S. Petrovic, Nikola D. Zivkovi2, Dušan M. Zivković, Diab etic oral Candidiasis, Acta Stomatologica,2011;27: 1025 – 1034.

23 Muhammad Jawed, Rashid N. Khan, SyedM. Shahid, and Abid Azhar, Protective Effects of Salivary Factors in Dental Caries in Diabetic Patients of Pakistan, Experimental Diabetes Research Volume 2012:1-5.

24 Shu-Fen Chuang,, Junne-Ming Sung, Shih-Chen Kuo, Jeng-Jong Huang, and Su-Yuan Lee, Oral and dental manifestations in diabetic and nondiabetic uremic patients receiving hemodialysis, Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005;99:689-95.

25 Silvia Martí Álamo, Yolanda Jimenez Soriano, M Gracia Sarrion Pérez, Dental considerations for the patient with diabetes, J Clin Exp Dent. 2011; 3(1):e25-30.

26 Abikshyeet P, Ramesh V, Oza N., Glucose estimation in the salivary secretion of diabetes mellitus patients, Diabetes Metab Syndr Obes. 2012; 5: 149-54.

27 L.Malathi, K.M.K. Masthan, N. Balachander, N. Aravindha Babu, E. Rajesh, Estimation of Salivary Amylase in Diabetes Patients and Saliva as a Diagnostic Tool in Early Diabetes Patients, Journal of Clinical and Diagnostic Research. 2013;7(11): 2634-2636.

28 Anđelski- Radičević Biljana, Mirković Silvija, Todorović Tatjana, Zelić Obrad, Changes in the biochemical composition of saliva in diabetic patients, Stomatoloski glasnik Srbije, 2006;53(4): 209-216.

29 Pacheco ECM, Reis LL, Dutra SMV, Rocha RF, Mancini MNG: Effects of the diabetes mellitus types 1 and 2 on the saliva secretion and composition in humans. Braz J Oral Sci, 2005; 4:854.

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