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Review Article

Oral Biofluid in Health and Disease – A Literature Review

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Abstract

Saliva is a biofluid that may be used for disease diagnosis, prognosis, and estimate risk in diseases. As the collection of saliva is non-invasive, simpler, the importance of salivary diagnostics has become the major area of research wherein saliva can be used to detect and quantify hormones, pro-inflammatory cytokine concentrations, levels of 2-HS-glycoprotein, salivary amylase, substance P, secretory IgA, cortisol and lysozyme antibodies, salivary sodium, salivary glucose, and several microorganisms. Saliva can also be tested for occupational toxins including lead and cadmium. The change in composition of saliva will be used in the detection of several systemic diseases such as hypertension, diabetes, Sjögren's syndrome, rheumatoid arthritis, systemic lupus erythematosus, and systemic sclerosis. Salivary diagnostics is a fast-developing field that uses saliva for early diagnosis, prognostics, and post-treatment monitoring of diseases. This article briefly overviews the normal and changes in salivary composition in diseased conditions.

Key words: Coronavirus, Oral diseases, Salivary biomarkers, Systemic diseases

INTRODUCTION

Saliva is a clinically useful biofluid that may be used for early illness diagnosis, prognosis, and risk stratification, as well as tracking therapy response in patients.[1] Saliva aids in protecting the intraoral structures from injuries caused by different pathogenic microbes, mechanical or chemical irritants.[2] Saliva quantity and quality can be affected by a variety of disorders and medical treatments. During illness, saliva composition and function are altered, allowing it to become a tool for the identification of many systemic diseases[3] [Tables 1 and 2]. Understanding saliva and its role in oral health can help health-care practitioners recognize the problems that might occur when saliva quantity or consistency is altered.[4]

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SALIVA AS A BIOMARKER

Biomarkers are measurable and have quantifiable biological characteristics which could be used to assess health and physiology, pathogenic processes, environmental factors, diagnose, assess illness prognosis, and identify pharmaceutical responses.[5]

Advantages

- Real-time diagnostic values.
- Non-invasive, simple, economical to collect, and screen samples at home.
- Cross contamination is rare.
- Samples, shipping, and storage are cost effective.
- The amount of manipulation required during diagnostic tests is lesser when compared to serum.
- Screening assays that are commercially available.
- Saliva, unlike blood, does not clot.[6]

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Table 1: Composition of saliva

Component	Glands	Cell type	Function
Serous glycoproteins PRP	Parotid and submandibular	Acinar cell	Prevent plaque formation, Ca 2+ binding, antimicrobial, lubrication
Mucous glycoproteins Mucins (MUC5B, MUC7)	Submandibular and sublingual	Acinar cell	Antimicrobial, lubrication, protease protective
Digestive enzymes α(alpha)-amylase	Parotid and submandibular	Acinar cell	Starch breakdown
Calcium-binding protein Statherin PRP	Parotid and submandibular	Acinar cell	Maintain tooth integrity inhibit Ca 2+ and *P* precipitation modulate bacterial binding
Antimicrobial proteins and peptides	Parotid and submandibular		
Lysozyme		Duct cell	Antimicrobial
Lactoferrin		Acinar cell	Antimicrobial and anti-inflammatory
Salivary peroxidase and myeloperoxidase			Antimicrobial, decomposition of H_2O_2
Cystatins		Acinar cell	Antiviral, protease inhibitors
Histatins		Acinar cell	Antifungal, antibacterial
Agglutinins Glycoprotein gp340	Parotid		Aggregate bacteria

PRP: Proline-rich protein

Table 2: Functions of saliva

Function	Description	Components
Lubrication	Coats, protects against mechanical, thermal, chemical irritation. Assists air flow, speech, and swallowing	Mucin glycoproteins
Cleansing	Moistening assists mastication, clearing food and swallowing	
Ionic reserve	Modulates demineralization and remineralization of teeth	Calcium phosphate, statherin, PRP
Buffering	Modulates pH of biofilm and buffering capacity of saliva	Bicarbonates phosphates, urea
Antibacterial action	Immunological agents and non-immunological agents help control oral microflora	IgA, IgG, IgM proteins, mucins, peptides and enzymes (lactoferrin, lysozyme, peroxidase)
Agglutination	Aggregate bacteria in saliva accelerating clearance from the oral cavity	Glycoproteins, statherin, agglutinins, histidine-rich proteins, PRP
Pellicle formation	Proteins form a protective layer on the teeth	Macromolecular proteins, statherin, histatins, cystatins, PRP, MG1
Digestion	Enzymes in saliva begin the breakdown of starch and fat	A-Amylase
Gustation	The solvent action and hypotonicity of saliva enhance tasting capacity by allowing interaction between nutrients and taste buds	Protein, gustin, zinc
Hydration	Oral dehydration and dryness of the mouth, stimulates desire to drink	

PRP: Proline-rich protein

The diagnosis of diseases is getting more difficult, necessitating the use of laboratory testing where salivary tests have greater sensitivity and correlation as a clinical tool over serum.[7,8] Several proteomic, transcriptomic, and microbiological markers been used in several oral and in systemic diseases which is discussed and given in [Flowcharts 1 and 2, Table 3].

ORAL DISEASE

Dental Caries

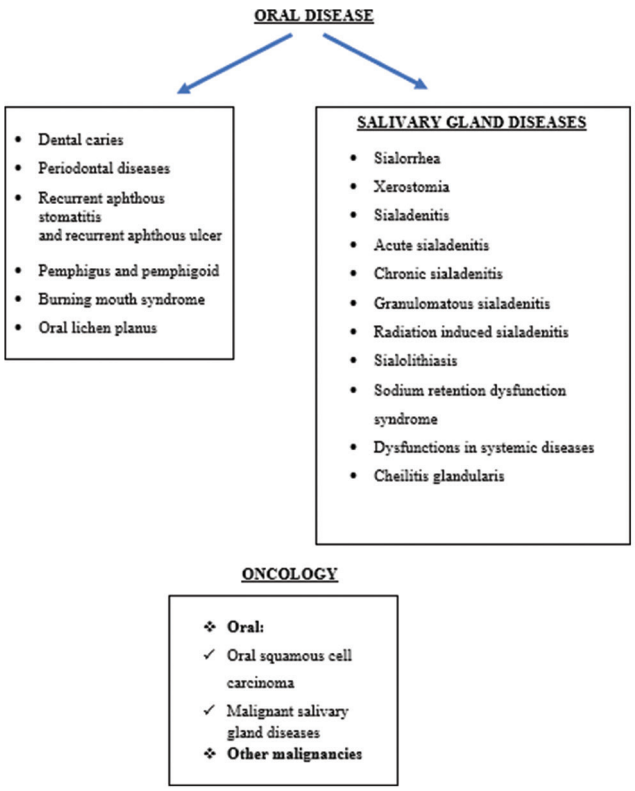
Streptococcus mutans and *Lactobacillus* in the highest levels indicate a transition in the oral microbiota from healthy to cariogenic.[7] Saliva in patients with lot of caries included more than 1×10^6 mL^{-1} of *S. mutans* and/or 1×10^5 mL^{-1} of *Lactobacillus* and low caries activity people contained 1×10^5 mL^{-1} of *S. mutans* and/or 1×10^4 mL^{-1} of *Lactobacillus*.[9] High amounts of proline (PRP1 and PRP3) and histatin 1 are high in caries-free people and statins cause a drop in high caries. Histatin S and statin are useful predictors for caries.[10]

Periodontal Diseases

Porphyromonas gingivalis has link to periodontitis and concentrations of 5×10^4–5×10^5 CFUmL1 produces results in under 90 min in saliva.[9] Increased levels of aspartate aminotransferase and alkaline phosphatase (ALP) have been linked to periodontal disorders. Using various methods, recent research is into the matrix metalloproteases (MMP), interleukins, hepatocellular growth factor, and TNF-G levels and in bone turnover biomarkers such as macrophage inflammatory protein-1G (MIP-1G), osteoprotegerin, and MIP-1G.[10]

Recurrent Aphthous Stomatitis and Recurrent Aphthous Ulcer

It is found that the levels of Vitamins A, C, E, and antioxidant (malondialdehyde-5) were shown to be considerably lower in patients.



Flowchart 1: Salivary biomarkers in oral disease conditions

Pemphigus and Pemphigoid

In vesiculobullous diseases, the presence of antibodies against epithelial tissue-specific adhesion molecules is noted. ELISA tests revealed that salivary desmoglein 1 and desmoglein 3 exhibited sensitivity of 70% and 94% in detecting pemphigus, respectively.

BURNING MOUTH SYNDROME

It is idiopathic but neuropathy has been possible etiology. The neuropeptides in the saliva in comparison with serum showed that calcitonin gene-related peptide reduced, substantial increase in NGF and mast cell products, drop in substance P, and no change in neutrophil markers in patients.[10]

Oral Lichen Planus (OLP)

In OLP, chronic inflammation is triggered using epithelial cell apoptosis mediated by autocytotoxic T lymphocytes. Cortisol, OS-related molecules, and cytokines are the protein-based biomarkers that have studied and pro-inflammatory mediators are significantly increased in OLP affected patients, that is, IL-4, IL-10, IL-18, TNF-α, NF-κB-related cytokines, CD44, and CD14.[11]

SALIVA IN SALIVARY GLAND DISEASES

Sialorrhea

Sialorrhea is a condition characterized by excessive saliva production. It can be associated with certain medications hyperhydration, infant teething, the secretory phase of menstruation, heavy metal poisoning, nausea, gastroesophageal reflux disease, obstructive, esophagitis, neuromuscular diseases, and neurologic changes such as in a cerebral vascular accident.[12-14]

Xerostomia

Xerostomia refers to the dryness of the oral cavity. These patients lack mouth lubrication due to diminished salivary flow and impair various activities by leading to infection.[15,16]

Sialadenitis

It is an inflammatory disorder of the salivary glands which is commonly caused by ductal obstruction with secondary bacterial infection as a result of reduced salivary flow and secretory stasis.[17,18] Acute and chronic sialadenitis is more susceptible to bacterial infections because its secretions are predominantly serous and lack the defense ingredients (IgA, sialic acid, and lysosomes) found in the mucinous secretions of the other salivary glands.[19]

Granulomatous Sialadenitis

It is most commonly caused by obstructive disease in which glandular parenchyma undergoes fibrosis after several recurrences and result in decreased salivary flow.[20]

Radiation-Induced Sialadenitis

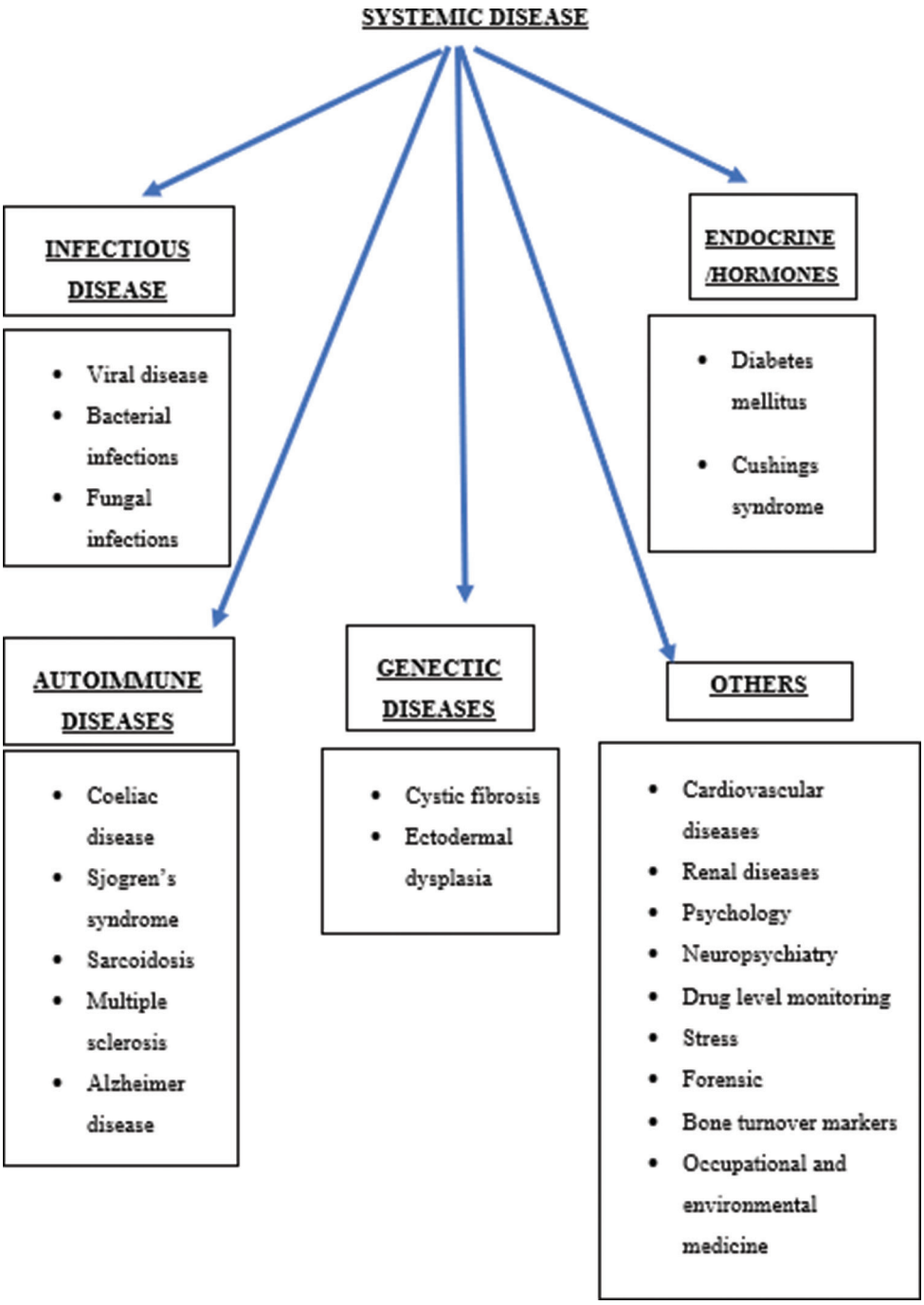
The salivary glands are frequently located within the area of external beam radiation that is used to treat head and neck tumors which results in low saliva production and appears viscous and ropy. They develop highly viscous secretions that can be difficult to clear from the throat.

Sialolithiasis

Sialoliths are calcified organic aggregates that occur within the main salivary glands' secretory pathway. These factors may cause pooling of saliva within the duct promotes stone formation. When a partial blockage of the duct occurs, the swelling subsides when salivary stimulation is eliminated, production drops, saliva seeps through the partial obstruction, and the calcium and sodium values in saliva alters.

Atresia

Absence or marked narrowing of the excretory duct of the salivary gland due to a congenital malformation of the first branchial arch is known as atresia where quantity of saliva is decreased leads to mucous retention or xerostomia.



Flowchart 2: Salivary biomarkers in systemic disease conditions

Diverticuli

A diverticulum is a pouch or sac that protrudes from the duct's wall. Saliva pooling and recurrent sialadenitis are caused by diverticuli in the ducts of the major salivary glands.

Sodium Retention Dysfunction Syndrome

In this situation, the typical proportional connection between salivary flow and salt concentration is disrupted. While most other chemicals are slightly raised, the sodium concentration is not only measured at lower flow rates but it is also relatively low and swings around a steady state of 2.5 mmol/L. Saliva can have a milky tint in some circumstances.[20]

Dysfunctions in Systemic Diseases

Reduced salivary flow, changes in salivary protein release, and irregularities in ductal electrolyte reabsorption are all symptoms of collagen vascular disorders connected to autoimmune diseases associated with Sjögren's syndrome. Diabetes mellitus causes salivary gland hypertrophy, protein modifications and salivary glucose levels are increased. In

Table 3: Salivary biomarkers in diseased conditions

DISEASES	SALIVARY BIOMARKER
Cardiovascular markers	Cardiac troponins, C-reactive protein, myoglobin, myeloperoxidase, ICAM-1, CD 40, and salivary lysozyme
Oncology	lnc RNA, miRNA, CCNI, EGFR, FGF19, FRS2 and GREB1, AGPAT1, B2M, BASP2, IER3, and IL1B, p53, CA15-3, C-erb2, CA 125, FGF 2, PSA, cortisol, lactate dehydrogenase, silver nitrate and nitrite, and salivary adenosine deaminase, glycoprotein CA 15-3, AZGP1, human calprotectin, epidermal growth factor, IL-1, IL-6, IL-8, TNF-α , Bacteria , ET-1 , TNF-α, IL-1α and IL-8 , CD44, IL-1β, IL-8, and calcium-binding protein S100, antibodies against the p53 gene, promoter hypermethylation of the p16 gene, VEGF
Infections • Viral infections • Bacterial infections • Fungal infections	Measles virus-specific IgM HIV – HIV-1, HIV-2 – antibodies, salivary proteins *Mycobacterium tuberculosis*, MUC 5B, and MUC 7 *Candidiasis* immunoglobulins, Hsp 70, and calprotectin, histatins, mucins, basic proline-rich proteins, and peroxidases, *H. pylori*, CMV
Coronavirus	Cytokines (IFN-a, IFN-g, IL-1b, IL-6, IL-12, IL-18, IL-33, TNF-a, TGF-b, etc.) and chemokines (CCL2, CCL3, CCL5, CXCL8, CXCL9, CXCL10, etc.)
Endocrinopathies • Cushing's syndrome	Cortisol
Diabetes mellitus	2-macroglobulin, (alpha)-defensins 1, 2, and 4, statherin, histatins 1 and 5, cathepsin D and MMP-9, IgA, salivary peroxidase, glucose content, potassium, salivary total protein, and amylase2
Renal diseases	Cortisol, nitrite, uric acid, sodium chloride, pH, alpha-amylase, and lactoferrin. Salivary phosphate, serum creatinine, and glomerular filtration rate
Genetic disorders • Cystic fibrosis • Ectodermal dysplasia	Cathepsin-D, sodium, potassium, chloride, calcium, magnesium, and lactate dehydrogenase Inorganic constituents, total protein
Autoimmune diseases • Sjogren's syndrome	Lactoferrin, beta-2 microglobulin, lysozyme C, cystatin C, Albumin serum, actin, alpha-actin-1, Ig gamma-1 chain C region, B2-microglobulin, Ig receptor polymeric salivary amylase, carbonic anhydrase, polymeric Ig receptor, prolactin-inducible protein, cystatin SN, calgranulin A and B, fatty acids protein binding, anti-transglutaminase, anti-histone, anti-SSA, and anti-SSB
• Multiple sclerosis	IgA production
• Sarcoidosis	Alpha-amylase and kallikrein
• Coeliac disease	Tissue anti-transglutaminase antibodies
Drug level monitoring	Nicotine, cannabinoids, cocaine, phencyclidine, opioids, barbiturates, diazepines, amphetamines, ethanol, cotinine, methamphetamine, endogenous γ-hydroxybutyric acid, and 3,4-methylenedioxymethamphetamine
Bone turnover markers	Body mass index, D-PYR, OC concentration, calcaneus T scores, hepatocyte growth factor, interleukin-1 beta, salivary osteonectin, and ALP activity
Dental caries and periodontal diseases	*Streptococcus mutans* and lactobacilli count, aspartate aminotransferase, alkaline phosphatase, uric acid, albumin, pIgR, Arp 3, CA VI, IL-1Ra, PLS-2, LEI, and IGJ
Stress	Salivary α-amylase
Forensic evidence	Blood group antigens and DNA testing
Occupational and environmental medicine	Salivary cortisol, IgA, lysozyme, chromogranin, alpha-amylase, lead, and cadmium
Psychology	Salivary amylase, cortisol, substance P, lysozyme, secretory IgG, and testosterone

hypertension, salivary sodium levels are declined. Alcoholic cirrhosis has reduced salivary flow rate with poorer electrolyte and protein levels. Cystic fibrosis has elevated protein, salt, chloride, calcium, and urea values.

Cheilitis Glandularis

It is a chronic inflammatory disorder that affects the minor salivary glands and their ducts resulting in abnormalities in the saliva flow mechanism and change in salivary composition leading thick saliva to produce from dilated ductal apertures.

ONCOLOGY

Oral Squamous Cell Carcinoma

Specific protein messenger ribonucleic acid (mRNA) levels are raised in the saliva of patients with head-and-neck cancer. Higher amounts of salivary nitrate, nitrite, and nitrate reductase activity are noted in oral cancers.[7] Salivary mRNA profiling revealed four important indications in persons with oral cancer (ILI-H, IL-8, ornithine decarboxylase antizyme-1, and spermidine N1 acetyl transferase). Saliva samples from patients with premalignant lesions (moderate or severe epithelial dysplasia) and cytokine IL-8 in patients with periodontal disease and autoimmune disorders, in addition to OSCC patients, showed higher levels of pro-inflammatory cytokines (IL-1, IL-6, IL-8, and TNF-α). Salivary fibroblast growth factor 2 and fibroblast growth factor receptor 1 concentrations are considerably greater in patients with salivary gland tumors, implying that saliva might be employed as a biomarker for early detection of salivary gland malignancies.[21]

Malignant Salivary Gland Disease

Several studies observed that maspin and stathmin exhibited higher levels of expression in adenoid cystic carcinoma of the salivary glands, which correlated to histologic grading in adenoid cystic carcinoma. Transketolase, modulator

recognition factor 2, Dim1p homolog, splicing factor (arginine/serine rich 9), and the v-Ha-ras l oncogene were found to be downregulated in poorly metastatic tumors and upregulated in highly metastatic tumors.[22]

Other Malignancies

Greater levels of the tumor markers c-erbB-2, cancer antigen 15-3, salivary levels of CA125, vascular endothelial growth factor, epidermal growth factor, and carcinoembryonic antigen were discovered in the saliva of women with breast cancer.[7,9] In pancreatic cancer, significantly higher amounts of hsa-miR-21, hsa-miR-23a, hsa-miR-23b, miR-29c, and hsa-miR-216 are noted in saliva. In prostate cancer, salivary PSA levels correlate with serum PSA levels.[8]

SYSTEMIC DISEASE

Cardiovascular Disease

Before and after cardiovascular surgery, salivary amylase activity was evaluated, and individuals with low salivary amylase had a larger death rate.[23] CRP has a plasma half-life of 19 h on average.[24] The levels of -2-HS-glycoprotein in saliva reduced, indicating that the peptidome could be used to help early diagnosis.[9] Acute myocardial infarction shows higher salivary soluble ICAM-1 levels, although salivary soluble CD40 ligand levels are much lower. In early stages, there are increased levels of salivary lysozyme associated with hypertension.

INFECTIOUS DISEASE

Viral Disease

At the proteome level, saliva-based antibody tests can detect viruses such as hepatitis A, B, C, HIV-1, measles, rubella, and vesicular stomatitis virus mumps virus, among others.[9] Western (immunoblot) assay paired with a nucleic acid-based viral load assay is used to confirm hepatitis virus infection. Quantitative DNA detection is used to assess the amount of virus in the body and to screen for hepatitis B surface antigen. OraSure, a point of care diagnostics, was analyzed and found to be an excellent approach for diagnosing HBV and hepatitis C virus.[25] PCR-based detection of virus DNA in saliva is a helpful approach for detecting HSV-1 reactivation early.[7]

Coronavirus Disease-19

It is a kind of viral pneumonia and is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Human coronaviruses (HCoVs) have been detected in the coronavirus (HCoV-229E and NL63) and coronavirus (MERS-CoV, SARS-CoV, HCoV-OC43, and HCoV-HKU1) families and the cytokine storm, a lethal uncontrolled systemic inflammatory response resulting from the release of enormous amounts of pro-inflammatory cytokines and chemokines. Up to 29 days after infection, some virus strains have been discovered in saliva that quickly differentiates for disease diagnosis.[26]

Bacterial Infections

Polymerase chain reaction is used to identify *Mycobacterium tuberculosis* when the bacterial count is high during the acute phase of the disease. MUC-5B and MUC 7, which are released by the mucous and serous acinar cells of the seromucous salivary glands, respectively, bind to pylori. Pneumococcal pneumonia ELISA detection of pneumococcal C polysaccharide in saliva is a useful supplement to detect pneumococcal pneumonia. Anti-tick antibody detection in saliva is used to identify Lyme disease. The sensitivity of *Taenia solium*-specific antibody to *Taenia solium* larvae in serum was higher than in saliva for detecting neurocysticercosis.[7,8]

Fungal Infections

In oral candidiasis, salivary fungal count analysis shows alterations in salivary proteins such as immunoglobulins, Hsp70, calprotectin, histatins, mucins, basic proline-rich proteins, and peroxidases. Fenn *et al.* showed that the salivary glucose level increased in diabetics leading to increased colonization of *Candida albicans* in oral cavity along with immunological alterations in the saliva.[27] *C. albicans* most commonly cause of oropharyngeal candidiasis.[28]

ENDOCRINE/HORMONES

Diabetes Mellitus

Diabetes is a metabolic condition that results in a glucose metabolism imbalance where levels of -2-macroglobulin in the saliva were found to have a positive connection with HbA1c indicating glycemic management in patients with type 2 diabetes.[9] In type 1 diabetes, (alpha)-defensins 1, 2, and 4 are up, while statherin, histatins 1 and 5 are down. Increased activity of proteases such as cathepsin D and MMP-9 allowing collagen fragments to be employed for monitoring diabetes-related disorders. Higher levels of IgA, salivary peroxidase, glucose content, potassium, salivary total protein, and amylase 2 are among the salivary changes.[23]

Cushing's Syndrome

Measuring cortisol in saliva is simple and reproducible and gives a reliable assessment of the hypothalamic-pituitary-adrenal axis. Salivary cortisol is in equilibrium with free cortisol in plasma and unaffected by the salivary flow.[21]

Monitory Levels of Hormones

Salivary testosterone monitoring can help with testicular function and behavioral studies concerning aggression, depression, abuse, violence, and antisocial activities.

Salivary progesterone levels correlated well with free serum levels, and greater salivary estriol is linked to an increased risk of premature delivery.[7]

RENAL DISEASES

Salivary markers associated with end-stage renal disease included nitrite, pH, sodium, chloride, uric acid, cortisol, alpha-amylase, and lactoferrin. Thus, salivary phosphate may serve as a superior marker than serum phosphate levels for diagnosis of heart disease and chronic renal failure.[8] The results of a similar study indicated that the salivary concentration of creatinine, urea, sodium, potassium, chloride, salivary urea, nitrogen, and G-amylase in patients with chronic renal failure was higher than in the control group while the calcium level was significantly lower.[10]

GENETIC DISEASES

Cystic Fibrosis

It is a hereditary disease caused by a mutation in the GFTR gene on chromosome 7's long arm.[10] This condition is characterized by abnormal electrolyte transport in epithelial cells and viscous mucus discharges from glands and epithelia. In the submandibular saliva, there was increase in electrolytes (sodium, chloride, calcium, and phosphorus), urea and uric acid, total protein, and lipids.[7]

Ectodermal Dysplasia

Ectodermal dysplasia is the X-linked hypohidrotic ectodermal dysplasia. The activity and the concentration of the alpha-amylase in the saliva were reduced.[8]

AUTOIMMUNE DISEASES

Coeliac Disease

Coeliac disease is a gastrointestinal disorder caused by hereditary susceptibility to gluten intolerance. Increase in peroxidase, myeloperoxidase, albumin, total protein, IgA, and IgG and a decrease in IgM and amylase in saliva are observed.[10] Salivary levels of 17-hydroxyprogesterone assessed by ELISA in the early morning are an appropriate screening test for the diagnosis of non-classic 21-hydroxylase deficiency.[7,10]

Sjogren's Syndrome (SS)

SS is a chronic autoimmune disease characterized by salivary and lacrimal gland dysfunction, keratoconjunctivitis sicca, xerostomia, and serological abnormalities.[7] Diagnosis of SS, sialochemistry is extremely useful.[23] SS is marked by a rise in immunoglobulins, inflammatory mediators, albumin, sodium, and chloride, as well as a decrease in phosphate. Lactoferrin, beta-2 microglobulin, lysozyme C, and cystatin C levels were shown to be higher in salivary protein analyses and salivary amylase, carbonic anhydrase levels were low.[9] They used ELISA to identify four salivary antibodies in separate patients (anti-transglutaminase, anti-histone, anti-SSA, and anti-SSB in primary SS), confirming the efficacy of highly active protein microarrays in salivary antibody detection as biomarkers.[21]

Sarcoidosis

Sarcoidosis is an inflammatory condition that affects the lymph nodes, lungs, liver, eyes, skin, and other organs. Decrease in saliva production volume, alpha-amylase, and kallikrein enzyme activity was noted. However, there was no link between the reduction in enzyme activity and the volume of secretion.[8]

Multiple Sclerosis (MS)

MS is an inflammatory disease that causes myelin loss and scarring where salivary diagnostics reveals no noteworthy changes except for a decrease in IgA production.[8]

Alzheimer Disease (AD)

In initial stages, there is decrease in acetylcholine levels that indicate cholinergic neuron loss. Salivary acetylcholinesterase (AChE) activity could be a valuable indicator of AD-related alterations in central cholinergic function and patient response to AChE inhibitor treatment.[25]

PSYCHOLOGY

The therapeutic responses in the treatment of anxiety can be measured with salivary 3-methyl-4-hydroxyphenyl glycol.[23] Salivary amylase, substance P, secretory IgA, cortisol, and lysozyme were discovered as salivary biomarkers. The amount of salivary amylase increases while the amount of secretory IgA decreases. Hsp 70, a salivary immune defense protein chaperone, has increased in levels. Testosterone levels in the saliva have been linked to aggressive behavior and physical activity.[8]

NEUROPSYCHIATRY

Dementia is a progressive cognitive decline that is accompanied by behavioral abnormalities. Aminotransferases and gamma-glutamyl transferase, ethanol, sialic acid, hexosaminidase A, and glucuronidase all found in saliva as markers for chronic alcoholism. Immune systems such as immunoglobulin A, peroxidase, and lactoferrin are disrupted due to chronic drinking. Lactotransferrin, Ig kappa chain C area, Ig gamma1 chain C region, Ig lambda-2 chain C region, neutrophil elastase,

and polymeric immunoglobulin receptor elevation and deletion in malignant brain tumors 1 noted in autistic individuals.[29]

DRUG LEVEL MONITORING

Nicotine, cannabis, cocaine, phencyclidine, opioids, barbiturates, diazepines, amphetamines, and ethanol are all detected in saliva. The drug is present in the saliva for the same amount of time as it is in the serum, therefore used for forensic reasons. Nicotine levels in saliva can be used to track tobacco smoke exposure.[8] Saliva may be used for monitoring antiepileptic and anti-cancer drugs.[7]

STRESS

Amylase (AAs), a salivary enzyme, has been proposed as a salivary marker that is sensitive to physiological alterations in response to stress. Cortisol reflects on hypothalamic-pituitary-adrenal axis activity.[30]

FORENSIC

In sexual abuse and harassment, genetic testing can be useful in identifying DNA in saliva. The foreign DNA can stay in the victim's saliva for up to 60 min, making it a useful piece of forensic evidence. During the biting action, saliva is deposited in sufficient quantities on the skin or object surface to allow DNA typing. DNA and mRNA, which help cells turn genetic information into proteins, can both be found in saliva.[7,8]

BONE TURNOVER MARKERS

Human saliva was tested for deoxypyridinium and osteocalcin and found correlated with calcaneus BMD/t scores. Alveolar bone loss has been linked to increased levels of ALP activity in periodontitis.[7,8]

OCCUPATIONAL AND ENVIRONMENTAL MEDICINE

Salivary cortisol levels are higher in chronic stress, while salivary IgA and lysozyme levels are lower. Acute stress signs include saliva chromogranin A and alpha-amylase. Cadmium concentrations in saliva are greater than in blood. The amount of lead found in saliva is only relevant to people who have been exposed to high amounts of lead poisoning.[8]

CONCLUSION

Saliva is a fluid secretion generated by the salivary glands making it a valuable diagnostic tool. Salivary biomarkers can help in screening and diagnosis as a point-of-care detection. It is a non-invasive sample collection method not only allows patients to receive repeated samples for long-term sickness monitoring but it also significantly reduces the pain and anxiety associated with blood analysis. As saliva is the mirror of the body with the use of saliva, several systemic diseases can be diagnosed at the early stage which reflects the health state of a person.

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