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Review Article

Salivary biomarkers an diagnostic tool for systemic and oral diseases - An review

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ABSTRACT:
Saliva is one of the tools that can non-invasively diagnose all oral and systemic diseases.Because saliva testing is intimately related to the oral cavity and other systems in our human body, clinical use of saliva testing for these conditions seems promising. Early detection of disease leads to better healing outcomes. Many diagnostic procedures are invasive and painful which gives unpleasant condition to the patients.With the invention of salivary biomarkers, saliva has become a ease diagnostic tool. Advances in saliva research have expanded the uses of saliva in diagnosis and achieved a expeditious development. In this review, we discussed various biomarkers in saliva that are used for early detection of oral and systemic diseases.A variety of biomarkers have been reported to function as diagnostic and prognostic tools for oral and systemic disease, but more research are recquired to identify and validate them.
Key word: Saliva, protein, diagnostic marker

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INTRODUCTION

Saliva is a promising liquid in the mouth. Saliva contains an enormous amount of information about the normal and abnormal processes of the body. Saliva is secreted from various major and minor salivary glands. Other than serum, saliva is one of the alternative diagnostic tool for various oral and systemic diseases. Saliva analysis does not require an invasive procedure and it is a convenient way to diagnose and predict oral diseases. Samples are easy to obtain and relatively easy to process, less complex in composition and more stable compared to other sources. [1]. It has been shown that saliva tests can be used to diagnose Coronavirus disease 2019(COVID-19) cost effectively during pandemic[2]. Saliva has impressive potential in the diagnostics of several systemic disorders and oral diseases.

SALIVA AND IT'S COMPOSITION

Saliva is a combination of mucosal exudate, salivary gland hyperosmotic fluid, and gingival crevicular fluid. Saliva lubricates the mouth, aids in chewing and digestion, and possesses antimicrobial qualities that make it useful as a buffer for foods that are acidic. Under healthy conditions, 0.75 to 1.5 L of saliva are produced daily. During the day, saliva secretion is still high but substantially decreases at night. Saliva is composed of 1% proteins, 99% water, (immunoglobulins,mucins, enzymes),inorganic materials, electrolytes and lipids [3].

ROLE OF BIOMARKERS

According to the National Institutes of Health (NIH), a biomarker is an objectively measured and evaluated indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to therapeutic intervention. Summarily, biomarkers are entities within the body capable of providing impartial information regarding the current physiologic state of a living organism[4].

Mass spectrometric technology advancements have ushered in a modern age for invention of biomarker that will have a significant impact on the detection and treatment of diseases in the future. More research

on salivary proteins revealed that saliva actually contains many aminoacids that, despite being available in varying levels , can play a critical role in the diagnosis of diseases.Theseaminoacids can be used as biomarkers for specific diseases. Although proteomes are crucial for diagnosis, salivary transcriptomic technology has succeeded in enhancing saliva's diagnostic capability for a variety of medicinal applications [5].

SALIVARY BIOMARKERS IN SYSTEMIC DISEASES

1. Cardiovacular disease:

Patients with cardiovascular disease have higher levels of the salivary biomarkers malondialdehyde (MDA) creatine kinase myocardial band (CK-MB), C-reactive protein (CRP), , and 2'7'dichlorodihydrofluorescein diacetate (DCFA-DA). Their observations of the changes in salivary levels of Troponin I (TnI), Matrix metalloproteinase-9 (MMP-9), Myeloperoxidase (MPO), B-type natriuretic peptide (BNP), Myoglobin and AdipoQ at the same time revealed significant disparities [6]. Atherosclerosis is associated with elevated salivary levels of TNF-α, Interleukin-6, Interleukin-1 beta and prostaglandin E2, which raises the possibility that these cytokines could serve as atherosclerosis biomarkers. An ECG associated with CRP levels successfully indicated acute myocardial infarction with a sensitivity of 80% and a specificity of 100%. creatine kinase myocardial band and Troponins were also found in saliva, although their diagnostic value was very low.[5].

2. Neurodegenerative disorders:

One of the common neurodegenerative disorders is Alzheimer's disease (AD). Alzheimer disease occurs in aged population. Saliva is used for alternative diagnostic tool for AD. Various studies have looked into the possibility of using saliva to measure AD markers including tubulin linked unit (TAU) and Amyloid peptide(Aβ) Aβ1–40,Aβ1–42 [7]. Several studies shown that lactoferrin an antimicrobial peptide used as an salivary biomarker for AD. Patients with AD also have higher amounts of the acetylcholinesterase (AChE) and pseudocholinesterase (PChE) in their saliva. [5].

Another common neurodegenerative disease is Parkinson's disease (PD**).** PD causes uncontrollable movements such as tremors, stiffnessand coordination difficulties. Salivary Biomarkers used for diagnosis of PD is alpha synuclein (α-synuclein),proteindeglycase(DJ-1),Hemeoxygenase(HO-1), cortisol and amylase. Patient with PD total α-synuclein levels are decreased while other biomarkers are elevated in saliva [7].

SALIVARY BIOMARKERS IN ORAL DISEASES

1. Periodontal disease:

Periodontitis is one of the most common non communicable disease in oral cavity. It is most commonly seen in aged patients. Patient with prolonged poor oral hygiene maintenance can cause periodontitis. In periodontitis salivary biomarkers are used to identify the phase of periodontitis. There are three phases of periodontitis. In Inflammatory phase, interleukin-1(IL-1), tumor necrosis factor-alpha (TNF-α), prostaglandin E2, and interleukin-6 (IL-6) are found in a high number. After the inflammatory phase, the disease progress and leads to elevarionof RANKL(Receptor activator of nuclear factor kappa-B ligand) tumor necrosis factor, and interleukin-1(IL-1),.

Interleukin 1 is an cytokine mostly involved in periodontitis, especially IL1β.Interleukin-1 promotes osteoclastic activity, which contributes to the bone loss associated with periodontitis, regulates the synthesis of prostaglandin E2, participates in the regulation of metalloproteinases and their inhibitors[5].LeveIs of IL1β are elevated in generalized periodontitis.Interleukin 6 (IL-6), which plays an vital role in the activity of immune cells and in the inflammatory response to the formation of bacterial plaque.. Among other cytokines elevated Interleukin 4 levels and reduced interleukin 17 levels.Another important biomarker associated with periodontitis is Matrix metalloproteinases(MMP). MMP 8 is an strong biomarker in saliva to detect the alveolar bone loss. Lira Junior et al. observed that elevated levels of MMP-8 in saliva were elevated in patients with aggressive periodontitis than in healthy persons.Increased salivary levels of matrix metalloproteinase-9 can also been detected. Increased levels of alanine aminotransferase (ALT) alkaline phosphatase (ALP), aspartate aminotransferase (AST) lactate dehydrogenase (LDH), also been associated with periodontitis[8].

2. Dental caries:

Dental caries is an highly widespread infectious condition in oral cavity. It is defined as an “irreversible microbiological disease of calcified tissues of teeth characterised by demineralised inorganic portion and destruction of organic substance of the tooth which often leads to cavitation”. Saliva act as an potential biomarker for diagnosis for dental caries. Biomarkers used for detection of dental caries Microorganisms such as Streptococcus mutans, lactobacilli, other microganisms such as Streptococcus sobrinus,actinomycesspp, candida albicans, salivary elctrolytes such as fluoride, calcium, phosphorus,zinc,iron, potassium,chloride Salivary proteins and peptide such as Immunoglobulin A, Immunoglobulin G and Immunoglobulin M ,Innate host defense proteins and peptides, Alpha amylase,Acidic proline-rich proteins, Agglutinins Mucous glycoproteins, Lactoferrin and lysozyme.

Functional properties of saliva also acts an biomarker such as Saliva flow rate, saliva pH, buffering capacity, sugar clearance rate [9].

3. Oral lichen planus:

Oral lichen planus is a potentially malignant oral disease. In oral lichen planus salivary cortisol levels are increased.Some studies indicate that stress can cause the recurrence of OLP. Cortisol has been proposed as a possible diagnostic marker for this disease. Among cytokines, Interleukin-6(IL-6),Interleukin-1(IL-1), Interleukin-4 (IL-4), andInterleukin-8 (IL-8), tumor necrosis factor α (TNF-α) have been described as important biomarkers for the diagnosis of Oral lichen planus. Both IL1α and IL1β levels are elevated in Oral lichen planus patients than in healthy individuals. The severity of Oral lichen planus has been linked to salivary levels of Interleukin-6 and Interleukin-8, although some authors have suggested that salivary Interleukin-8 is a more reliable Oral lichen planus biomarker.[8].

4. Sjogren's syndrome:

Sjögren's syndrome (SS) is an autoimmune condition that causes dry mouth and dry eyes.Sjogren's syndrome patients have altered salivary content and a reduced salivary flow rate.(8). In saliva several alterations in transcriptomes and proteome can used to diagnose sjogren's syndrome. Biomarkers used for diagnosis for sjogren's syndrome is Salivary Beta 2-Microglobulin (β2m), Salivary Lactroferrin, , Salivary Carbonic Anhydrase VI, Salivary Soluble Sialic Acid-Binding Immunoglobulin-like Lectin (Siglec)-5, Salivary Neutrophil Gelatinase-Associated Lipocalin (NGAL),Salivary Adiponectin, cytokines such as Tumor Necrosis Factor-α (TNF-α), Interleukin-17A, Interleukin-6 and Salivary autoantibody such as Anti-Muscarinic type 3 receptor (M3R),parotid secretory protein (PSP) antibodies,anti-SSA, and anti-SSB antibodies[10].

CONCLUSION

Saliva is an important diagnostic tool for systemic and oral diseases. It has a good chance for early diagnosis of systemic and oral diseases. Collecting samples from saliva is quiet easier than from serum. This review discusses biomarkers in saliva for several systemic and oral diseases.One would want complex studies so that the saliva could detect the disease earlier.

CONFLICT OF INTEREST

Nil

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