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COMPONENTS OF SALIVA FOR DIAGNOSIS OF DIFFERENT DISEASES

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ABSTRACT

In oral diagnostics, it has been a great challenge to determine biomarkers for screening and predicting the early onset of disease (prognostic tests) or evaluating the disease activity and the efficacy of therapy (diagnostic tests). An oral diagnostic tool, in general, should provide pertinent information for differential diagnosis, localization of disease and severity of infection. It serves as a basis for treatment planning and provides a means for assessing the effectiveness of therapy. Saliva is simple, non-invasive, readily available and easily collected without specialized equipment or personnel. For the past two decades, saliva has been increasingly evaluated as a diagnostic fluid for detecting breast cancer , oral cancer , caries risk, salivary gland diseases, periodontitis , and systemic disorders such as hepatitis C and the presence of human immunodeficiency virus (HIV).

KEY WORDS: Saliva, Diagnostic agent, Diagnosis, Diseases.

INTRODUCTION

Saliva is a watery substance located in the mouths of humans and animals, secreted by the salivary glands. Human saliva is 99.5% water, while the other 0.5% consists of electrolytes, mucus, white blood cells, epithelial cells (which they can use to extract DNA), glycoproteins, enzymes (such as amylase), antimicrobial agents such as secretory IgAand lysozyme.[1,2] Saliva is a clinically informative, biological fluid (biofluid) that is useful for novel approaches to prognosis, laboratory or clinical diagnosis, and monitoring and management of patients with both oral and systemic diseases. It is easily collected and stored and ideal for early detection of disease as it contains specific soluble biological markers (biomarkers). Saliva contains multiple biomarkers which make it useful

for multiplexed assays that are being developed as point-of-care (POC) devices, rapid tests, or in more standardized formats for centralized clinical laboratory operations. Salivary diagnostics is a dynamic field that is being incorporated as part of disease diagnosis, clinical monitoring and for making important clinical decisions for patient care.[3,4]

Historically, systemic diseases are diagnosed via (1) patient reported symptoms, (2) examination and a medical history obtained by a physician or other medical professional, (3) chemical analysis of blood and/or urine samples. Now a days there has been increasing interest in the use of saliva, and other oral samples, for the diagnosis of oral and systemic diseases.[5] As a diagnostic fluid, saliva offers distinctive advantages over serum because it can be collected non-invasively by individuals with modest training. Furthermore, saliva may provide a cost-effective approach for the screening of large populations. Gland-specific saliva can be used for diagnosis of pathology specific to one of the major salivary glands. Whole saliva, however, is most frequently used for diagnosis of systemic diseases, since it is readily collected and contains serum constituents.[6]

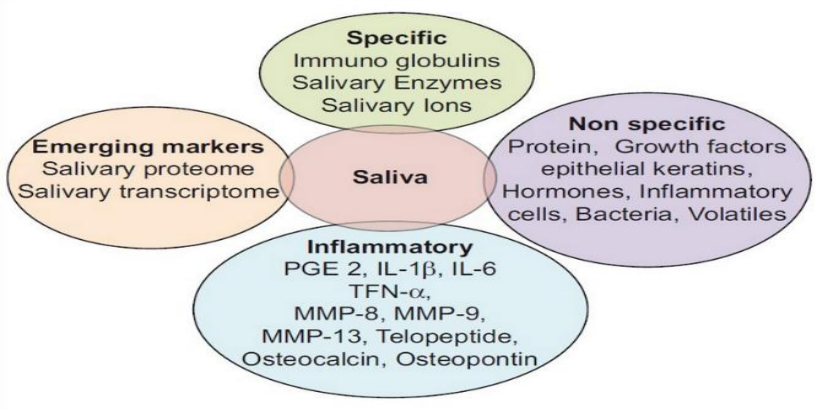

Fig: Saliva Components

DIAGNOSIS OF DISEASES BY USING SALIVA

The ability to monitor health status, disease onset, progression, and treatment outcome through noninvasive means is a highly desirable goal in health care promotion and delivery. Saliva is a perfect medium to be explored for health and disease surveillance.[7-9] Efforts on the discovery of analytes in the saliva of normal and diseased subjects suggest an additional function of saliva, a local and systematic diagnostic tool. Oral samples are useful for the diagnosis of systemic diseases such as saliva. Saliva is simple, non-invasive, readily available and easily collected without specialized equipment or personnel.

Analysis of saliva done for the diagnosis of following: 1. Early morning salivary levels of 17-hydroxyprogesterone (17-OHP) determined by ELISA is an excellent screening test for the diagnosis of non-classic 21-hydroxylase deficiency, since the salivary levels accurately reflected serum levels of 17-OHP.[10] 2. Autoimmune diseases Sjögren's syndrome — Sjögren's syndrome (SS) is an autoimmune exocrinopathy of unknown etiology. Serum chemistry can demonstrate polyclonal hypergammaglobulinemia and elevated levels of rheumatoid factor, antinuclear antibody, anti-SS-A, and anti-SS-B antibody. In addition, increased concentrations of sodium and chloride, IgA, IgG, lacoferrin, and albumin, and a decreased concentration of phosphate were reported in saliva of patients with SS.[11]3. Malignancy Salivary analysis may aid in the early detection and screening of certain malignant tumours. Saliva also aids in monitoring the efficacy of treatment. The mRNA levels for specific proteins are elevated in the saliva of head and neck cancer patients. p53 is a tumour suppressor protein which is produced in cells exposed to various types of DNA-damaging stress. Inactivation of this suppressor through mutation is considered a frequent occurrence in the development of human cancer. Accumulation of inactive p53 protein occur, which in turn lead to the production of antibodies directed against this p53 protein.The p53 antibodies can be detected in the saliva of patients diagnosed with oral squamous cell carcinoma (SCC), and can thus assist in the early detection and screening for, this tumour [12]4. Defensins Elevated levels of salivary defensin-1 were found to be indicative of the presence of oral SCC. high-positive correlation was observed between salivary defensin-1 levels and serum levels of SCC-related antigen.[13] 5. Viral Diseases HIV Antibody to HIV in whole saliva of infected individuals was detected by ELISA and Western blot assay, correlated with serum antibody levels [14]. Salivary IgA levels to HIV decline as infected patients become symptomatic. It was suggested that detection of IgA antibody to HIV in saliva may, therefore, be a prognostic indicator for the progression of HIV infection. Analysis of antibody in saliva as a diagnostic test for HIV (or other infections) offers several distinctive advantages when compared with serum. 1. Saliva can be collected non-invasively, which eliminates the risk of infection for the health care worker who collects the blood sample. 2. Furthermore, viral transmission via saliva is unlikely, since infectious virus is rarely isolated from saliva. 3. Saliva collection also simplifies the diagnostic process in special populations in whom blood drawing is difficult, i.e., individuals with compromised venous access (e.g., injecting drug users), patients with haemophilia, and children several salivary and oral fluid tests have been developed for HIV diagnosis. Orasure is the only FDA-approved, commercially available testing system. It detects antibodies against the p24 antigen

of HIV. Collection and analysis of saliva offer a simple, safe, well-tolerated, and accurate method for the diagnosis of HIV infection. Applicable for both clinical use and epidemiological surveillance.[15]6. Hepatitis Saliva was found to be a useful alternative to serum for the diagnosis of viral hepatitis. Acute hepatitis A (HAV) and hepatitis B (HBV) were diagnosed based on the presence of IgM antibodies in saliva. Hepatitis B virus DNA revealed by PCR in saliva. Quantitative detection of DNA used to evaluate level of virus in the body copy for judgement of infection. It also point to the possible role of saliva as a source of HBV infection.[16, 17] 7. Measles, mumps, and rubella Saliva may also be used for determining immunization and detecting infection with measles, mumps, and rubella.[18] Rotavirus For newborn infants, the salivary IgA response was found to be a better marker of rotavirus (RV) infection than the serum antibody response. 8. CA15-3, c-erbB-2 Elevated levels of recognized tumour markers c-erbB-2 (ERB) and cancer antigen 15-3 (CA15-3) were found in the saliva of women diagnosed with breast cancer, as compared with patients with benign lesions and healthy controls.[19] 9. CA 125 is a tumor marker for cancer. Elevated salivary levels of CA 125 were detected in patients with untreated breast cancer than healthy controls and patients who were treated for breast cancer.[20] 10. Infectious diseases Saliva contains immunoglobulins (IgA, IgM, IgG) that originate from two sources: the salivary glands and serum. Antibodies against viruses, bacteria, fungal and parasite can be detected in saliva and can aid in the diagnosis of infections. Helicobacter pylori infection has been associated with peptic ulcer and chronic gastritis.[21] 11. Pneumococcal pneumonia the detection of pneumococcal C polysaccharide in saliva by ELISA may offer a valuable complement to conventional diagnostic methods for pneumococcal pneumonia. Quantitative measurement of pneumococcal capsular antigen in the saliva may be valuable in helping to make an aetiological diagnosis in children with pneumonia.[22] 12. Lyme disease is caused by the spirochete Borrelia burgdorferi and is transmitted to humans by blood-feeding ticks. The detection of anti-tick antibody in saliva serves as a screening mechanism for individuals at risk for Lyme disease.[23] 13. Taenia solium Specific antibody to Taenia solium larvae in serum demonstrated greater sensitivity than antibody in saliva for identification of neurocysticercosis.[24] 14. Non invasive diagnosis of amebic liver abscess is challenging, detection of E. histolytica DNA in saliva by real. antibodies could be used to monitor the immune response to vaccination and infection with RV.[25] 15.Reactivation of herpes simplex virus type-1 (HSV-1) is involved in the pathogenesis of Bell's palsy and PCRbased identification of virus DNA in saliva is a useful method for the early detection of HSV-1 reactivation in patients with Bell's palsy.[26] 16. Dengue is a mosquito-transmitted viral

disease. Salivary levels of anti-dengue IgM and IgGs demonstrated sensitivity of 92% and specificity of 100% in the diagnosis of infection. So, detection of dengue specific salivary IgG and IgM antibodies is useful markers for dengue infection.[27]

Advantages Of Saliva as a diagnostic agent[28, 29]

1. Noninvasive diagnosis of disease and monitoring of general health.
2. Painless, patient suffers no discomfort and little anxiety in the collection process.
3. Simple in collection with a modest trained assistant and applicable in remote areas.
4. Relatively cheap technology as compared to other tests.
5. Cost effective applicability for screening large population.
6. Can be used to study special population where blood sampling is a problem e.g children, anxious /handicap/ elderly patients.
7. Convenient for multisampling.
8. Safer for health professionals than blood tests.
9. Compared to blood and urine, saliva is also cheaper to store and ship.
10. In addition saliva does not clot and can be manipulated more easily than blood.

CONCLUSION

Although blood is still the gold standard for diagnostics of diseases and drugs, Saliva offers an alternative to serum as a biologic fluid for diagnostic purposes. The components of saliva act as a—mirror of the body's health, and the widespread use and growing acceptability of saliva as a diagnostic tool is helping individuals, researchers, health care professionals and community health programs to better detect and monitor disease and to improve the general health of the public. Analytes used for disease detection range from proteins, to antibodies, and nucleic acids that are of either human microorganism origins. Highly sensitive and high-throughput assays such as mass spectrometry, RT-PCR, microarray, and nano-scale sensors that can measure proteins and nucleic acids with a minimal amount of sample requirement in a short period of time allowed scientists to broaden the utility of saliva as a diagnostic tool. The noninvasive nature and ease of collection have made saliva the fluid of choice for not only diagnostic but also the more important health surveillance purposes.

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