Saliva : Diagnostic Tool of Future ???

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Abstract

Saliva compared to blood, in regards to parameters such as sensitivity, specificity, collection, expense and patient compliance, stands out. Saliva is increasingly being used as ao diagnostic tool not only for various autoimmune, infectious, endocrine diseases but it can also acts as a potential biomarker for oral cancer detection. Salivary diagnosis has gained its popularity due to its non invasive collection technique. Saliva is being termed as the "diagnostic fluid of the future".

Through this review, we wish to provide an update on the role of saliva as a diagnostic and prognostic tool of the future.

Introduction

Saliva is one of the most complex secretion having versatility in function and composition. It is an important biological fluid, meeting a vast range of physiological needs."[1] Blood will always be a primary biofluid for diverse diagnostic tests, but it has distinct limitation and disadvantage.[1] Saliva fulfills several of the chief diagnostic concerns for a diagnostic biofluid because of its sensitivity, collection, expense, patient compliance, time saving etc.[1,2]

Interest in the saliva has increased over time period and it has been studied extensively. Saliva is filled with hundreds of components that may serve to detect various systemic disease or provide evidence of exposure to various harmful substances, as well as act as a source of various biomarkers.[1] Early detection of life threatening condition by the use of saliva as a biomarker, enhance survival rate of the patient and result in better prognosis and this is the main attraction of using saliva as a diagnostic tool.[1]

Materials & Methods of Collection of Saliva

Saliva can be collected under stimulated or unstimulated conditions. In unstimulated state the parotid, submandibular, sublingual and minor salivary glands contributes approximately 25%, 60%, 7%-8% and 7%-8% respectively, to the whole saliva volume. Stimulation affects the quality of saliva, the concentrations of some constituents and the pH of the fluid. Normal whole saliva secretory rate varies between 800 and 1.500 ml/day with a pH in the range of 6.0-7.0. Stimulations affects the quantity of saliva, the concentrations of some constituents and the pH of the fluid.[3] **(Fig. 1)**

Whole mouth resting saliva can be collected by, the draining/drooling method, the spitting method, the swabbing method and the suction method.[1]

Stimulated saliva is collected either by asking the patient to chew a piece of paraffin or by applying 0.1-0.2 mol/lit citric acid on tongue.[4]

Collection of pure glandular secretions is possible with the use of special collection devices, for example the Lashley-cup for collection of parotid saliva.[1]

Functions of Saliva

Saliva has several functions that are found to be important for individual oral health.[4] (Table 1)

In Dentistry saliva has an important role to play in the initiation, progression and a prognosis of both dental caries and periodontitis. Of all the properties of saliva, its viscosity is directly related to the dental caries which results in an increase in the incidence of dental caries. Whereas the capability of drawing thread of a fluid or its spinnbarkiet can predict the extent and severity of periodontitis in a patient.[5]

Viral Diseases- Saliva can be used to detect antibodies to various viruses like[1] (Table 2)

1. Hepatitis- Saliva can been utilized to detect even very low levels of antibodies to HAV, associated with vaccine-induced immunity. Excellent results have been demonstrated on comparison of serum and saliva levels of infection and vaccine-induced HAV-specific IgG. On comparing oral fluids to serum the sensitivity and specificity was reported to be 100% for the detection of HB surface antigen and antibodies to HCV, respectively. As previously reported the commercially available serological kit yields a sensitivity of 92% and specificity of 86.8%.[1]

2. Dengue- Salivary levels of anti-dengue IgM, demonstrates a sensitivity of 90.3% and a specificity of 92.0%, hence representing that salivary IgM is a useful diagnostic marker for DEN infection.[1]

3. Human Immunodeficiency Virus (HIV) - Researchers have proved that the diagnosis of infection with the HIV, based on specific antibody in saliva, is equivalent to serum in accuracy, and therefore is applicable for both clinical use and epidemiological surveillance.[4] As compared with serum, the sensitivity and specificity of antibody to HIV in saliva, for detection of infection, are between 95% and 100%.[4] Hence can be a better tool for screening of patients.[1]

Systemic Diseases may result in alteration of various components of saliva.

1. In Diabetes Mellitus some authors have found that there was not any statistically significant concentration of glucose which was present in the saliva of diabetic patient as compared to a healthy one.[12] Whereas some authors found that the glucose levels in saliva was significantly higher in diabetic patients as compared to non-diabetic ones.[1] Studies also showed that EGF concentration was significantly lower ($p<0.05$) for the diabetic patients as compared to the control patients. The reduced levels of salivary EGF in diabetic patients are said to be contributory factors in the development of the oral and systemic complications of diabetes and this may future clinical applications.[1]

2. In Parkinson's disease it was observed by researchers that the amount of saliva production in patients of Parkinson group was significantly lower than in controls group (0.68±0.26 mg vs. 1.27±0.65 mg, respectively; $p=0.009$), also the salivary concentrations of sodium, potassium, and chloride were higher, but that of amylase was lower than in controls ($p=0.02$, $p<0.001$,

p=0.003, p=0.04, respectively).[3]

3. In Myocardial Infarction the biomarkers like C-reactive protein, soluble CD40 ligand, myeloperoxidase, myoglobin, tumor necrosis factor, soluble intercellular adhesion molecule-1 and matrix metalloproteinase 9 show significant alteration in the saliva of subjects with myocardial infarction as compared to normal subjects.[1]

Autoimmune Diseases which result in the formation of auto antibodies can also be detected through saliva for example-

Sjogren's Syndrome (SjS) which shows salivary and lacrimal dysfunction, the anti-Ro60 autoantibodies were detected in the saliva of 70% of SjS patients with 96% specificity. Positive anti-Ro60 autoantibodies were also found in 70% of the matched serum samples (96% specificity). The Luciferase Immunoprecipitation System (LIPS) detected Ro52 autoantibodies in the saliva and serum of 67% of SjS patients with 100% specificity.[1]

In Infectious Disease Like Tuberculosis 98% detection rate of Mycobacterium tuberculosis was obtained by polymerase chain reaction (PCR) using mixed saliva, in contrast to a 17.3% detection rate by cultivation.[7]

In Pneumococcal Pneumonia- The detection of pneumococcal C polysaccharide in saliva by ELISA, demonstrated a sensitivity of 55% and specificity of 97%.[1]

Early detection of any malignant lesion may result in better prognosis of the patient and in a reduction of morbidity and mortality.[1]

A most important result found in the study done by Shpitzer is that all eight salivary parameters analysed in the cancer patients were altered in a highly significant manner, and were characterised by relatively high sensitivity and specificity values. Five of these were increased in the cancer patients by 39 246%: carbonyls, Ki67, CycD1, MMP-9 and LDH (Pp0.01). The other three markers were decreased in the cancer patient by 16 29%: OGG1, Maspin and phospho-Src (P0.01).[2]

Breast Cancer- Elevated levels of recognized tumor markers c-erbb-2 (erb) and cancer antigen 15-3 (CA15-3) were found in the saliva of women diagnosed with breast carcinoma, as compared with patients with benign lesions and healthy controls. Senstivity and specificity of salivary c-erb B-2 protein were 87 % & 65 % respectiviely.[1]

Ovarian Cancer- CA 125 is a tumor marker for epithelial ovarian cancer. Elevated salivary levels of CA 125 were detected in patients with epithelial ovarian cancer as compared with patients with benign pelvic masses and healthy controls. Saliva demonstrated a somewhat lower sensitivity than serum (81.3% vs. 93.8%, respectively); however, the specificity and positive predictive value were higher for saliva vs. serum (88.0% vs. 59.8% and 54 . 2 % vs 2 8.8 %, respectively.[1]

Leukemia- The oral manifestations of leukemia's occur early in course of disease & these oral features can at times act as a diagnostic indicatior. A rise in salivary amylase levels in leukemic patient has been reported in patients suffering from Leukemia(p<01).[1]

Saliva in Forensic Sciences

Saliva plays a major role in forensic sciences. This includes evaluation of chemical markers (thiocynate ion, amylase), serological markers (blood group substances, macro molecular glycoproteins) for individual identification and of substance abuse, sex determination and DNA analysis.

Advantages of Salivary Diagnosis

Saliva collection is inexpensive and it is easy to collect, store, ship. Moreover it can be collected by little armamentarium. Various advantages of salivary diagnosis are given in the Table No. 3.[3]

Table 3. Advantages[1,2]

1. It is easily accessible.
2. Accurate.
3. Less expensive.
4. Its collection is safer than blood tests which could expose health care workers to HIV or hepatitis virus.
5. Since it does not clot, not time consuming.
6. Requires minimal training.
7. Used for mass screening of large population.

Conclusion

Saliva contains many markers which are connected with each other and alterations in these markers indicates that they belong to a single network. Changes in these salivary markers may be used as a diagnostic tool for diagnosis, prognosis and post operative monitoring.

References

References are available on request at editor@healtalkht.com

Table 1. Functions of various components of saliva[4]

Functions	Components
Lubrication	Mucin, proline rich glycoproteins, water
Antimicrobial action	Lysozyme, lactoferrin, lactoperoxides, mucins, cystins, histatins, immunoglobulins, proline rich glycoproteins, IgA
Maintaining mucosal integrity	Mucins, electrolytes, water
Cleansing	Water
Buffer capacity and remineralisation	Bicarbonate, phosphate, calcium, staterin, proline rich anionic proteins,fluoride.
Preparing food for swallowing	Water, mucins
Digestion	Amylase, lipase, ribonucleases, proteases, water, mucins
Taste	Water, gustin

Table 2. Saliva has long been used for the monitoring of various diseases [1]

1	Viral disease	Hepatitis HIV Dengue
2.	Systemic disease	Diabetes Melitis Parkinsons Myocardial Infarction
3.	Autoimmune Disease	Sjogren Syndrome
4.	Infectious Disease	Mycobacterium Tuberculosis Pneumococcal pneumonia
5.	Cancers	Squamous cell carcinoma Breast Cancer Ovarian Cancer Gastric Cancer

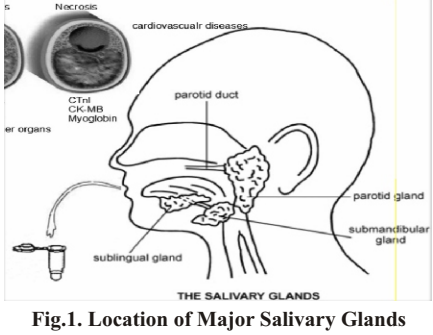

Fig.1. Location of Major Salivary Glands in the Oral Cavity.