Salivary Bio fluid: A Window to Human Health

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Abstract:- **Salivary diagnostics is a rapidly developing field using nanotechnology and molecular diagnostics to helporal & systemic diseases. The term Salivaomics was coined in 2008 and includes study of genomics, transcriptomics, proteomics, metabonomics and microRNA (miRNA) analysis in saliva. Due to quick advancement in saliva omics, saliva is well documented as a pool of biological markers. Saliva is a non-invasive and safe source, which can be an alternative for blood in the diagnosis and prognosis of diseases. This review summarises various salivary tests used for diagnosis of oral & systemic diseases by detecting their specific biomarkers.**

Keywords:- *salivaomics , proteomics , salivary tests, diagnostic tool, COVID 19.*

I. INTRODUCTION

Salivary diagnostics, which was once a far vision is now a leading tool in diagnostic. Timely diagnosis of disease is the key to prevent complications which have anadverse impact on quality of life. Researchers all over the world are constantly working towards finding a diagnostic tool which is non-invasive, specific, economical, easy to perform & require less manipulation during diagnostic procedure. Saliva as diagnostic tool fulfil all these requirements & thus has now emerged as a revolutionary tool in diagnostics.Saliva,99% water & 1% of digestive enzymes, proteins & inorganic substances such as, mucopolysaccharide, salivary amylase,lysozymes andmucin, and some inorganic matter such as K+,Na+, Cl−,Ca2+ and the thiocyanate ion. Salivary glands being extremely permeable &encircled by capillaries allows free exchange of blood derived biomolecules vis transcellular or paracellular routes[1].Thus biomarkers released in blood reachsaliva & provide molecular information capable of conveying an individual's current health status.Owing to the upscale in salivary researches the concept of salivaomics has been conceived. Salivaomics includes transcriptomics, proteomics,genomics,microRNA (miRNA) analysis andmetabonomics[2]. Salivaomics term was coined in 2008 and is used for the development of knowledge about the salivary constituent. Salivaomic Knowledge Base (SKB) developed by Dr.Wong[3] manages all the research related to salivaomics& is the only online platform dedicated to it. Early diagnosis of disease is an important aspect of health management. Tests which can diagnose a disease while even in asymptomatic stage will be a boon to human health. Salivary diagnosticsis a step forward towards this goal.

Saliva as a diagnostic fluid has been studied as early as 1967 for detecting cystic fibrosis[4]. The main limitation to salivary diagnostics earlier was less concentration of analytes incontrast to blood but with the development innanotechnology&extremely sensitive molecular methods this is now no longer a limitation to salivaomics . Various oral and systemic disease which can be detected using saliva are as follows –

A. *Oral –*
   a) Dental caries
   b) Periodontal diseases
   c) Sjogrens disease
   d) Oral Cancer

B. *Systemic –*
   e) Diabetes Mellitus
   f) Cardiovascular diseases (Acute myocardial infarction)
   g) Asthma
   h) Chronic obstructive pulmonary disease
   i) Viral diseases:
      i) HIV
      ii) Hepatits C
      iii) COVID 19

Along with all the diseases mentioned above certain systemic conditions such as pregnancy, chronic tobacco use, halitosis can also be detected by identifying their respective biomarkers. National Institutes of Health (NIH) defined biomarker as an objectively measured and evaluated indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to therapeutic intervention. [5]

Table 1 gives a comprehensive view about the disease detected& the test used or the diagnosis of these diseases[6,7]. Table 2 gives a detailed insight to chairside salivary based detection tests for periodontal diseases.[8]

With the new paradigm shift in diagnostic era saliva is now being used to detect COVID, ICMR has now validated few test kits like COVID-19 antigen rapid card test (ORAL SALIVA),MERISCREEN COVID-19 Ag test kit-V.1,BIOCARD Pro COVID-19 Antigen Saliva Kit,BIOCARD Pro COVID-19 Antigen Saliva Kit (Table 3) although these kits have not been approved yet but still it's a big step towards the future.[9] In a recent study by Teo et al [10] in 2021 they have concluded saliva as a less intrusive andsensitivesample for COVID-19 diagnosis.

C. *Limitations of salivaomics:*
Concentrations of certain markers in saliva are not every time a reliable reflection of the levels in serum as the salivary composition can be affected by the collection method and degree of stimulation of saliva. Salivary flow rate changes may affect the level of salivary markers and their availability due to salivary pH change.Various medications, Systemic disorders&radiation can affect salivary gland function and accordingly the composition & quantity of saliva. Proteolytic enzymes and oral microorganismscan affect the stability of diagnostic markers.[11]

II. CONCLUSION

Saliva being non-invasive, specific, easy to perform & economical is emerging as a new tool for diagnosis of

diseases. Oral & systemic diseases both can be diagnosed at an earlier stage by detection of specific biomarkers. The level of biomarkers in saliva is comparative to the level in blood as the salivary glands are highly permeable. Diseases such as periodontal diseases, diabetes, myocardial infarction, HIV, COVID -19 can easily be diagnosed at early stages. Limitations of salivary diagnostics include change in salivary composition due to medication, radiation therapy. Thus, further studies are required to enhance the diagnostic capability of saliva.

S.no	Disease	Test	Salivary biomarker
1	Diabetes	Screen-printed electro chemical sensor	Glucose
2	HIV	Oraquick	Hiv-1/2 antibody
3	Hepatitis c	Mono-lisa anti-hcv plus	HCV antibody
4	Acute myocardial infarction	Luminex lab-on-a-chip	C-reactive protein, myoglobin, mmp-9, il-1b, slcam-1, myeloperoxidase
5	Asthma & chronic obstructive pulmonary disease	Multiplexed fiber optic microsphere-based cytokine array	Ifng, IP-10, tantes, eotaxin-3, VEGF
6	Periodontitis	Table 2	MMP-8, IL-1b, C-reactive protein
7	Pregnancy	Salistick	Hormone beta-HCG
8	Halitosis	Bana test	Microbial-enzymatic n-benzoyl- dl- arginine-2-napthylamide
9	Tobacco use	Nicalert test strips	Cotinine

Table 1: Salivary tests for oral & systemic diseases and conditions

	Test kits	Basis	Technique	Biomarker detected	Accuracy
Microbiological tests	Evalusite	Sandwich enzyme immunoassay (colorimetric assay)	Antigen based sandwich immunoassay	Aa, Pg, Pi	Specificity – 98% Aa Sensitivity – 28%
	Perioscan		Hydrolysis of a synthetic trypsin substrate, N-benzoyl-DL-arginine-2-naphthylamide	Bacteroides forsythus, Pg, Treponema denticola as Well as certain Capnocytophaga species that produce trypsin-like Enzyme	Sensitivity of 99% Specificity of 55%
	Omnigene (dmdx)	DNA hybridization	Nucleic acid technology genomic probe characterisation of virus species of all genome type including Aa, Pg, Pt, Fn, Td, Ec	Aa, Pg, Pi	96% sensitivity and 86% specificity for Aa
	IAI Pado Test 4.5	DNA hybridization	Uses oligonucleotide probes complementary to conserved fragments of the 16S r-RNA gene (codes for subunit of bacterial ribosome)	Aa, Pg, Tannerella Forsythia, and T. Denticola	
Biochemical tests	Myperiopath				
	Perio-Check (Ac Tech)	Enzymatic digestion reaction (colorimetric assays)	Detects proteases such as collagenases, elastases, and proteinases in GCF using insoluble dye-labeled collagen fibrils	In gingivitis levels increase	Sensitivity of 88% and a specificity of 61%
	Prognos-Stik (Dentsply)		Detects the Presence of serine proteinase elastase in GCF sample	Detects active disease sites	
	Periogard	Enzymatic digestion reaction (colorimetric assays)	Levels of enzyme Aspartate aminotransferase (AST) in GCF sample	Markers of early periodontal tissue destruction Discriminate between sites with Severe inflammation but with no attachment loss from sites With attachment loss.	
	Pocketwatch	Enzymatic digestion reaction (colorimetric assays)	Analyzes aspartate transaminase	Distinguish between Active and inactive sites	
	Perio 2000 System		Volatile sulfide Compounds (VSCs) directly degrade periodontal Structures aggravating periodontitis, their evaluation can indicate The subgingival microbial load	Pg, Pi and T. Forsythia Produce sulfates	
	Dip Stick Test		Detects matrix metalloproteinase-8 (MMP-8) by immunochromatography principle		
Genetic tests	Periodontitis		Evaluates the simultaneous occurrence of allele 2 at the IL-1 α+4845 and 1β +3954 loci	Identifys Individuals at risk for	

| | | | | severe periodontal disease even before The age of 60. | |
| Myperio ID | Genetic polymorphisms detection | Targets genes for IL-6 / IL-1 | | Patient's genetic Susceptibility to periodontal diseases. | |

Table 2: Chairside salivary tests for periodontal diseases

S.No	Developer	Name of Kit	Country
1	Bhat Bio-Tech India (P) Ltd.	COVID-19 antigen rapid card test (ORAL SALIVA)	India
2	Meril Diagnostics	MERISCREEN COVID-19 Ag test kit-V.1	India
3	Capital Health Services India Private Limited	LFA for antigen detection test-deep throat saliva specimen	India
4	Trivtron Health Pvt. Ltd., Chennai	BIOCARD Pro COVID-19 Antigen Saliva Kit	India
5	Real-Time Analyzers Inc,USA	CoviSaliva Antigen Test Kit	USA
6	Sensing Self Pte.Ltd	S1 Covid-19 Rapid Antigen Test Kit	Singapore

Table 3: Saliva bases COVID detection tests

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