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Salivary Diagnostics in Oral and Systemic Diseases - A Review

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Abstract:- Salivary diagnostics, an emerging field in medical research, leverages the analysis of saliva for non-invasive detection, monitoring, and management of various diseases. This abstract explores the potential of saliva as a diagnostic fluid, highlighting its advantages such as ease of collection, cost-effectiveness, and patient acceptability compared to traditional blood or tissue sampling. Key biomarkers identified in saliva include proteins, nucleic acids, and metabolites that reflect systemic health conditions, oral diseases, infectious agents, and even systemic diseases like cancer and diabetes. Advances in technology, such as biosensors and genomic analysis, enhance the sensitivity and specificity of salivary diagnostics, paving the way for personalized medicine and early intervention strategies. Challenges including standardization, variability in saliva composition, and regulatory approval are also discussed, underscoring the need for further research and clinical validation. Salivary diagnostics holds promise as a valuable tool in future healthcare, potentially transforming how diseases are diagnosed and managed globally.

Keywords:- *Saliva, Biomarkers, Oral and Systemic Diseases.*

I. INTRODUCTION

Saliva is a complex and dynamic biological fluid composed of various secretions such as the salivary glands, the sweat of the oral mucosa and the gingival sulcus. Compounds derived from blood and other substances from the gastrointestinal and respiratory systems are known to be present in salivary secretions. This varies from person to person, but is also used to identify specific symptoms of bacteria, viruses or systemic diseases, drugs, hormones, impurities, etc. It is less invasive than blood or tissue samples and is quick and easy to collect. Transport, storage and treatment.

Salivary biomarkers, molecules found in saliva that reflect physiological or pathological processes in the body, appear as valuable tools in various areas, such as medicine, dentistry and research. This introduction examines the importance of salivary biomarkers in medical progress and highlights their potential applications in clinics and research [1, 2].

II. COMPOSITION

Saliva is composed of a variety of electrolytes, including Sodium, potassium, calcium, magnesium, bicarbonate and phosphate. Other molecules in saliva include immunoglobulins, proteins, enzymes, mucins, and nitrogenous products such as urea and ammonia. The function of each ingredient is as follows: (1) Bicarbonate, phosphate and urea contribute to pH control and anti-inflammatory properties. (2) Macromolecular proteins and mucins participate in purification, synthesis, and adhesion to oral microorganisms and participate in signal metabolism. (3) Magnesium, phosphate, and protein work together as anti-mineralization factors and control remineralization and remineralization. (4) Immunoglobulins, proteins and enzymes provide antibacterial activity.

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Salivary components, especially proteins, are multifunctional (perform more than one function), macroscopic (have similar functions but at different rates), and amphibious (function in activities that are beneficial to the host). Recent studies on the complex functions of salivary proteins and mucins support this theory [2].

Saliva is a very thin liquid that is 99% water. Initially, saliva is isotonic as it forms in the acini, but becomes hypotonic as it moves through the tubular network. The hypotonicity of unstimulated saliva allows taste buds to detect various tastes without being masked by normal plasma sodium levels. Especially during periods of low flow, hypotony can cause swelling and dehydration of the mucin glycoproteins that protect oral tissues. Low levels of glucose, bicarbonate, and urea in unstimulated saliva enhance the hypotonic environment and enhance taste.

The normal pH of saliva is 6-7, slightly acidic. The pH of salivary flow ranges from 5.3 (low flow) to 7.8 (high flow). The major salivary glands account for most of the secretory volume and electrolyte content of saliva, while the minor salivary glands secrete little and release most of the blood group substances [3].

III. FUNCTIONS

Saliva is responsible for the initial digestion of starch in the presence of salivary amylase or ptyalin. Saliva keeps the mouth moist, making swallowing easier and keeping the mouth comfortable. Saliva dissolves food molecules so that the taste receptors on the tongue can detect the taste. It creates a lump that makes swallowing easier and helps food move through the digestive tract. Saliva contains antibiotics and antibiotics to prevent oral infections and protect against harmful bacteria. Saliva helps regenerate dental plaque, neutralize acids produced by bacteria and wash away food particles, reducing the risk of tooth decay and gum disease [4].

IV. ADVANTAGES OF SALIVARY DIAGNOSTICS

Saliva collection is non-invasive and painless compared to blood tests or tissue biopsy, making it more convenient for patients, including children and the elderly. It can be collected easily and conveniently in various environments without the need for special equipment or trained medical personnel. This makes it suitable for home testing or in remote areas with limited access to healthcare compared to blood tests or other invasive procedures, as it requires fewer resources to collect and process. Samples can be collected. several times over time, allowing regular monitoring of biomarkers or disease progression without causing discomfort to the patient. A saliva sample contains various biomarkers (eg, hormones, antibodies, DNA) that can reflect oral health as well as systemic diseases. These biomarkers are often stable in saliva and can provide reliable diagnostic information. Unlike taking blood samples, the risk of spreading the infection through saliva is minimal, which increases the safety of diagnostic procedures. Many patients prefer saliva testing because of its simplicity and disadvantages. -invasive nature, which can lead to better compliance with testing recommendations. Salivary biomarkers allow early detection of diseases or conditions before symptoms appear, allowing for earlier intervention and potentially better treatment outcomes [5].

V. SALIVARY BIOMARKERS IN ORAL DISEASE

Saliva, carries specific markers like enzymes and proteins from the body that can signal the existence and intensity of gum diseases such as gingivitis and periodontitis. Higher amounts of these markers in saliva are linked to inflammation and damage to the gums and surrounding bone. It can be examined for markers related to the risk of tooth decay, such as the count of mutans streptococci, lactobacilli, and the ability to buffer. These markers assist in pinpointing people at a greater risk for tooth decay, enabling focused prevention strategies. Biomarkers of saliva have demonstrated potential in the early detection of mouth cancers. Biomarkers like the composition of salivary proteins, DNA changes, and certain proteins can signal the existence of mouth cancer or early signs of cancer. This non-invasive method could lead to earlier treatment and better outcomes. Salivary biomarkers can track the development of mouth diseases and how well treatments are working. For instance, shifts in mouth fluid biomarkers can show how patients are reacting to gum treatments or if oral lesions are coming back after treatment. Saliva hosts a wide variety of bacteria that make up the oral microbiome. Alterations in the mix and variety of these bacteria, as seen through mouth fluid biomarkers, can offer clues about oral health issues, including gum diseases, tooth decay, and oral infections [6].

Table 1 Salivary Biomarkers in Oral Diseases [7, 9].

Disease/Pathology	**Biomarkers/proteins**
Oral lichen planus	Cortisol (increased levels), nitric acid (increased levels), CRP(increased levels), INF-ALPHA(increased levels), IL1, IL8(increased levels)
Oral leukoplakia	TNF-alpha(increased),IL6,IL8,IL10,IL37, LDH,TGF,EGF
Periodontitis	CRP(increased levels), TNF-alpha(increased/decreased levels), IL1,IL4,1L6,RANKL,OPG,MIP-1,OSC,ALP, LDH, AST,ALT(increased levels)
Medication related osteoradionecrosis of jaw	IL6, IL1, IL1RA,MMP9(increased levels)
Primary Sjogren’s syndrome	CD44, B2M, SP1, PSP, CA6IL12(increased levels)
Peri-implantitis	TNF-alpha,IL1(increased levels)

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VI. SALIVARY BIOMARKERS IN SYSTEMIC DISEASES

Salivary biomarkers for systemic diseases are seen in patients with various conditions. These biomarkers can be used as an indicator of the respective systemic disease and aids in the further treatment plan.

Table 2 Salivary biomarkers in systemic diseases [8].

Disease/Pathology	**Biomarkers/proteins**
Rheumatoid arthritis	GRP78/BiP
Acute myocardial infarction	MMP-8, C-RP, MPO, CKP, CK-MB, CARDIAC TROPONIN T
Gastric diseases	High levels of MUC5B, MUC7
Acute coronary syndrome	Cathepsin L
Systemic sclerosis	Salivary psoriasin(s100A7)
Primary biliary cholangitis	AMA-M2
Breast carcinoma	CA15-3, c-erbB-2, Cathepsin- D, p53
Colorectal cancer	TIMP-1
Resectable pancreatic cancer	Salivary MicroRNA
Early pancreatic cancer	Salivary HOTAIR and PVTI
Parkinson’s disease and progressive supra-nuclear palsy	Salivary alpha-synuclein
Pancreatic cancer	miR-3679-5p, miR-940, KRAS,MBD3L2, ACRVI-1, DPM1
Lung cancer	Cytokine(IL1RN, IL1B,IL6, IL7, IL8,IL10, CCL1, TNFCXCL10)
Gastric cancer	Glycoproteins, RNA(SPINK-7, PPL, SEMA4B)

VII. TECHNOLOGICAL ADVANCES IN SALIVARY DIAGNOSTICS:

New technologies for measuring biomarkers in saliva are revolutionizing disease diagnosis and precision medicine today (**Figure 1**). Microfluidic chip devices can measure many more disease biomarkers in real time with greater sensitivity and specificity. Microfluidics is recognized as a powerful technology platform with a wide range of applications in diverse fields such as biology, biomedicine, chemistry and the environment. These microfluidic devices (**Figure 2**) are prepared from organic and inorganic solvents of various materials. But most of the materials are not compatible universally. To solve this problem, multiple methods of measuring multiple biomarkers can be combined to jointly define a true marker for a disease state. Artificial intelligence is a useful tool to detect and automatically detect these phenomena, especially as new technologies generate more molecular data. The amount of obtained biomarker data is classified and predicted by artificial intelligence. Artificial intelligence and its ability to recognize disease-specific patterns in data is critical to exploiting the new molecular information that can be extracted from microchip-based diagnostic programs. "Small data" in the development of new water biotechnologies has presented challenges for the development of artificial intelligence techniques, but these challenges can be overcome through careful research and design and careful use of current algorithms. By combining multiple molecular biomarker measurements, AI has been shown to improve diagnostic performance compared to manually selected biomarkers used in the underlying datasets. AI algorithms can simultaneously assess the effects of multiple biomarkers and discover advanced interactions between biomarkers that cannot be designed manually. Because, these technologies are more mature for clinical use, the datasets are much larger than liquid biopsy. The continued development of artificial intelligence and its application in the field of saliva analysis and microfluidic chip devices will continue to promote the trend of saliva analysis generating datasets on automated microcomputers [10, 11, 12].

VIII. CHALLENGES AND FUTURE DIRECTIONS:

Salivary exposure has been shown to be a surrogate for serum protein biomarkers. Saliva collection sites have different effects on different biomarkers. In many scientific areas, such as randomized controlled trials, many sampling and statistical errors occur when processing samples from healthy volunteers. The amount of saliva and the biochemical composition of a person is influenced by age, sex and diet. Age and salivary flow are related to salivary α-amylase activity in healthy individuals. Saliva collection is quick, easy and painless, making this sample a simple tool for diagnostic testing. However, sample collection must be optimized to minimize errors. For example, collection methods and collection time can influence the determination of cortisol activity and salivary amylase activity. Collection and processing methods affect the measurement of total protein concentration and CRP and immunoglobulin concentrations [13]. Many factors (for example, the method of measurement and the standards used) can affect the results obtained from saliva evaluation. Salivary biological responses are also influenced by the method of collection. These factors include the method of saliva collection (can be passive stimulation (passive drooling), stimulation, spitting, scraping and suction) and the type or degree of stimulation of saliva flow (mechanical and/or gustatory). Important differences in experimental design. In fact, salivary flow rate is the most important factor in determining salivary biomarkers and is also determined by many factors such as fluid status, stress response, age, genetic influence, drug composition, and changes and daily effects. The rate of salivation is also different in healthy people. Due to volume variation between individuals, salivary flow and other biological parameters may vary between individuals. First,

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the disadvantages associated with saliva arise primarily because most saliva collections are performed by spitting directly into the tube or tube pad, thereby altering the sample compared to blood. Second, the sampling method is not sterile and samples are susceptible to bacterial contamination over time. Third, drugs that are administered orally and can be inhaled (eg, methamphetamine, marijuana, cocaine) may not be detected because drug residues remaining in the mouth may be overestimated in saliva samples after recent use. Drug concentrations must be measured accurately because they may not reflect blood drug concentrations. As saliva screening research continues, there is a need to improve sensitivity, specificity, repeatability, and correlation with current diagnostic criteria. Saliva is a biological fluid with scientific and clinical potential. Advances in saliva sensing technology are changing applications from disease diagnosis to health screenings [14, 15].

IX. CONCLUSION

This review outlines the information found in current literature and explores the importance and potential of saliva in identifying different tissue and organ-related diseases early on, potentially leading to personalized medicine advancements. Saliva diagnosis has proven to be effective in identifying diseases such as cancer, with correlation to clinical diagnosis. Continued research could establish it as a biomarker for determining the histological grading and clinical stage of the disease. Additionally, this review has verified the clinical efficacy of using saliva for evaluating systemic diseases. By examining the information provided above, we can easily grasp the extensive use of saliva within the medical industry. Recent studies have discovered that saliva has the ability to indicate shifts in both physical well-being and mental functions throughout time. Additionally, it can serve as a marker for preventing and diagnosing diseases. In the meantime, this review indicates the importance of conducting experiments that impact saliva testing in the ultimate prediction outcomes.

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FIGURES

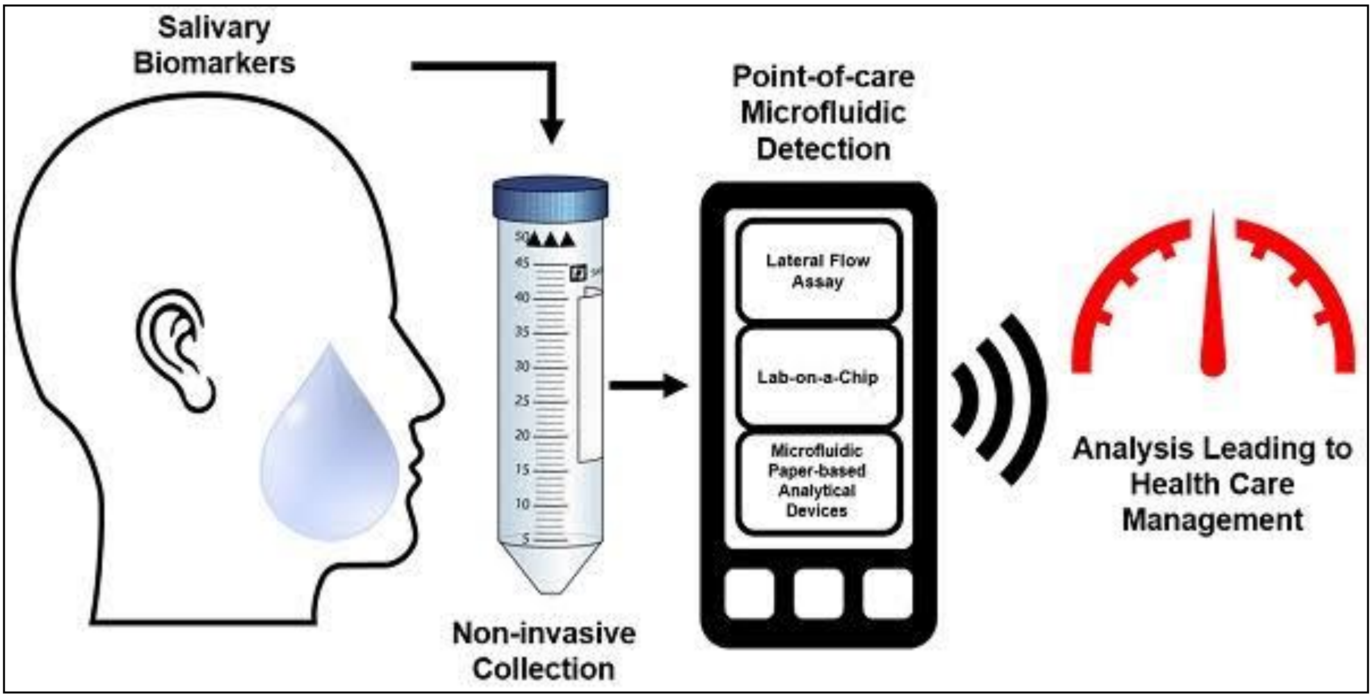

Fig 1Point of Care Analysis.

Fig 2 Micro-Fluidic Chip for Salivary Analysis.