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Salivary Marker And Cardiovascular Disease

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ABSTRACT:

Human saliva plays a crucial role infood digestion and maintaining oral hygiene. Components of saliva constituting the electrolytes, mucus, glycoproteins, enzymes, various antibacterial compounds, and gingival crevicular fluid provides the optimum condition both of oral cavity and general health. Fortunately collection of this amazing fluid is very easy and non invasive. These particular advantages only make saliva a potential diagnostic fluid. Through detailed analysis, an array of salivary proteins and peptides found which may be beneficial as biomarkers in oral and systemic diseases. So by this review, we discuss the importance of human salivary proteomes and tabulate the recent salivary biomarkers found in subjects with acute myocardial infarction and other systemic disease. Since acute myocardial infarction contributes to large cases of mortality worldwide,especially in a clinical setting, an early detection using these biomarkers can provide an effective solution to decrease the global heart attack incidence particularly among the high-risk group of type-2 diabetes mellitus patients. Currentchallenges in saliva collection are also mentioned which need to be improved, resulting in better quality of saliva samples and produce biomarkers for future use in clinical applications.

KEYWORDS: *Liquid biopsy, saliva, biomarkers, Acute Myocardial Infarction.*

INTRODUCTION: Over the last decade, human saliva has been getting attraction attention as a liquid biopsy from various scientists for detection of common oral diseases like dental caries, gingivitis, periodontitis (both chronic&aggressive), Bechet disease, even carcinoma like oral squamous cell carcinoma, developmental defects like cleft palate and lips, salivary gland diseases, premalignant diseases like oral leukoplakia, chronic graft-versus-host disease (cGVHD), and systematic diseases such as breast cancer, diabetes, human immune deficiency virus (HIV). Biomarkers are rightfully described as biological molecules found in blood, saliva and other body fluids, or tissues which are a sign of a normal or abnormal process, or of a condition or disease. These biomarkers are divided as follows-strong (S), questionable (Q) and potential (P). Though majority of the biomarkers are tested and found positive in the serum, not all can be detected in blood. But on the contrary many of these biomarkers enter saliva via blood either through passive diffusion, active transport or extracellular ultra-filtration. So, saliva can be a good expression of the physiological function of the body [1]. Collection of this miracle fluid iseasy, non-invasive, totally painless, rapid collection can be carried out and at the same time cost effective too. Minimum training required to collect the sample.So, this gradual advancements in "*omics*" sciences toward salivary research will aid in identification of biomarkers related to healthy and diseased state [2].Saliva possesses biomarkers obtained from serum, gingival crevicular fluid, and mucosal transudate which are useful in multiplexed assays that are being developed as point-of-care devices, rapid tests, or in more standardized formats for centralized clinical laboratory operations [7]. The efficiency and accuracy of these proteomic technologies can make it possible in future to turn salivary diagnostics into a clinical reality.

SALIVARY BIOMARKER IN DETECTION OF CARDIOVASCULAR DISEASE

BIOMARKERS: Myoglobin (MYO), Cardiac troponin I (cTnI), Creatine phosphokinase MB (CK-MB), Myeloperoxidase (MPO), brain natriuretic peptide (NT-proBNP), Exosomal miRNA, C-Reactive Protein (CRP), Matrix metalloproteinase-8 (MMP-8), MMP-9 and tissue inhibitor of MMP-8 (TIMP-1)[3-8]

MYOGLOBIN : Myoglobin, which found in both serum and saliva bio-fluids, can be utilized to detect AMI. Miller and his coworkers conducted research, and mentioned that salivary myoglobin levels were greater within 48 h of the onset of angina in AMI patients [1].

CARDIAC TROPONIN I: It was proved that the unstimulated saliva concentration of Cardiac troponin-I (cTnI) at the onset of 12 h and 24 h of Acute Myocardial Infection

CK-MB: Creatine phosphokinase-MB (CK-MB) increased in patients with AMI compared to Non-AMI controls.

CRP is one of the inflammatory mediators of our body that is produced to trigger the complement cascade in response to acute injuries and infections. It also contributes and plays a vital role in atherogenesis [1]. Studies proving a group of salivary biomarkers including CRP, MYO, and MPO as a diagnostic tool for AMI have shown a sensitivity of 90–100% [9,10]. Various researches were made to test and check the compatibility of salivary biomarkers with serum biomarkers [1,11]. Labat et al. In his investigation found a strong, positive and significant relation between salivary and serum CRP levels among patients with ischemic heart disease (IHD). Certain specific cardiac biomarkers and non-specific inflammatory biomarkers having significant roles in inflammation and plaque instability were studied by Kossaify et al where they deduced levels of CRP, CK-MB, cardiac troponin I, cardiac troponin T, some interleukins (IL), tumor necrosis factor alpha (TNF-Alpha), MMPs, and MPO are all associated with both saliva and serum [5]. The alteration in the levels of the biomarkers particularly correlated to heart tissues like myocardial injury, myocardial inflammation and myocardial stress. Folley et al. also analysed the use of unstimulated whole saliva to detect cardiovascular health. They did study on Unstimulated whole saliva and the serum was collected from 29 patients with Cardio Vascular Disease in an interval of 0.8, 16, 24 and 48 h post invasive cardiac procedures, by gingival and sublingual swabs. Results depicted the biomarkers which are in serum also can be found in saliva, thus ultimately suggesting that saliva can provide an essential tool for assessing cardiac ischemia or necrosis [12]. Among all these proteins, natriuretic peptides, C-reactive protein (CRP), creatine kinase (CK), and cardiac troponin were included as commonly used cardiac biomarkers in acute cardiac care [16]. A kit for measuring human salivary CRP, a common biomarker which is related to cardiovascular inflammation, has been developed by Salimetrics® for clinical settings. Recent another technology i.e cutting-edge technology called Oral Fluid NanoSensor Test (OFNASET) which is portable, cheap, accurate, definitive, and quantitative results. Besides its intended use in oral cancer, this particular alternative can possibly benefit the point-of-care multiplex detection of salivary biomarkers among AMI patients [17]. So as being mentioned above about the clinical benefits of collection of saliva, the salivary proteome of patients should be very useful in identifying the heart condition of the patient thus possible also to detect or predict AMI. These discoveries may increase the diagnostic utility of salivary proteomes as biomarkers in relation to CVD, but unfortunately none of the salivary biomarkers mentioned above have been verified to predict the onset of AMI. In future, there is bright probability that these newly obtained salivary biomarkers may provide an early molecular diagnosis and increase the survival rate of cardiovascular patients as opposed to that of plasma. However, more studies and validation regarding this needed in order to find discriminatory biomarkers for this disease.

CHALLENGES : Saliva diagnostic tests has the potential to be utilized within a varied range of clinical applications which includes population-based screening programs, confirmatory diagnosis, risk stratification, prognosis determination, and therapy response monitoring. Older age often associated with a number of cases related to functional limitations, heart failure, prior coronary disease, and renal insufficiency [13]. As a result, saliva collection can be a challenge among older T2DM patients. For example, geriatric patients are prone to xerostomia upon medications with anticholinergic properties, dehydration, diabetes, and radiotherapy for head and neck cancer [14]. Dry mouth in elderly patients are common complications which can limit the amount of sample collected and compromise its subsequent results. Some alternative sample collection approaches been there such as passive drool, filter paper, and microsponges but each individual methods has its own

advantages and disadvantages in terms of sufficient sample recovery [15]. The researchers has to select the best methods according to the patients and also in accordance to the nature of research.

SUMMARY OF ADVANTAGES AND DISADVANTAGES OF SALIVA AS DIAGNOSTIC FLUID:

ADVANTAGES:

- Collection methods are non-invasive and cost effective
- Risk of contacting deadly pathogens while handling saliva is minimal.
- Sampling is convenient for both practioner and patient.
- No preprocessing technique is required to prevent clotting, unlike blood.

DISADVANTAGES:

- Collection methods are not completely standardized in terms of different physiological states and types of commercial kits.
- Samples may be contaminated with blood from oral mucosa and periodontal lesions due to inflammation.

CONCLUSION:

The interest in diagnosis based on salivary analysis has been growing from over past decade. Due to its simplicity and non-invasiveness in collection procedure salivary biopsy is becoming popular. Saliva collection is relatively painless, easy for the practitioners to convince the patients at the same time early diagnosis and frequent monitoring the patients becomes possible. The sensitivity and specificity of a salivary test can be considered equal to that of blood. Most important advantage be the cheap collection and safety for both the practitioner and patient. With the help of that, early diagnosis of patients especially from developing countries becomes easy with minimal costs but achieving great precision. Detailed analysis of human salivary proteome by various methods though necessary in order to find the most productable markers for later utility in acute cardiac care.

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