ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 11, Issue – 3, June – 2026, Page No. : 54 – 61

Salivary Biomarkers: Unlocking The Diagnostic Power of Saliva

[1]Dr. Arani Datta, Post Graduate Trainee, Department of Oral and Maxillofacial Pathology and Microbiology, Gurunanak Institute of Dental Sciences and Research, Panihati, Kolkata -700114, West Bengal, India

[2]Prof. Dr. Mousumi Pal, MDS (CAL), Ph. D (WBUHS), Professor and Head, Department of Oral and Maxillofacial Pathology and Microbiology, Gurunanak Institute of Dental Sciences and Research, Panihati, Kolkata -700114, West Bengal, India

[3]Dr. Sanjeet Kr. Das, MDS(WBUHS), Ph. D Scholar (JIS University), Associate Professor, Department of Oral and Maxillofacial Pathology and Microbiology, Gurunanak Institute of Dental Sciences and Research, Panihati, Kolkata -700114, West Bengal, India

Corresponding Author: Dr. Arani Datta, Post Graduate Trainee, Department of Oral and Maxillofacial Pathology and Microbiology, Gurunanak Institute of Dental Sciences and Research, Panihati, Kolkata -700114, West Bengal, India

Citation this Article: Dr. Arani Datta, Prof. Dr. Mousumi Pal, Dr. Sanjeet Kr. Das, "Salivary Biomarkers: Unlocking The Diagnostic Power of Saliva", IJMSIR – June – 2026, Vol – 11, Issue – 3, P. No. 54 – 61.

Type of Publication: Review Article

Conflicts of Interest: Nil

Abstract

Saliva has become a promising diagnostic biofluid due to its non-invasive collection methods, cost efficiency, and capacity to reflect both oral and systemic physiological conditions. Recently, there has been a growing focus on utilizing salivary biomarkers for diagnosing and tracking various systemic diseases. Saliva comprises a wide range of biomolecules, such as proteins, enzymes, hormones, antibodies, nucleic acids, metabolites, and electrolytes, many of which enter saliva from serum through processes like passive diffusion, active transport, or ultrafiltration across the salivary gland epithelium. These components can indicate pathological changes occurring in various organs and systems throughout the body. Developments in molecular biology, proteomics, genomics, and metabolomics have enabled the discovery of many salivary biomarkers specific to certain diseases. Although there are some limitations, including differences in salivary composition, flow rates, and the possibility of contamination, saliva presents considerable promise as a trustworthy substitute. Therefore, the exploration and validation of salivary biomarkers could revolutionize early disease detection, disease monitoring, and personalized healthcare.

Keywords: Saliva, Non-invasive, Biomolecules, Salivary Biomarker.

Introduction

Saliva has gained increasing recognition as a diagnostic biofluid due to its non-invasive collection, ease of handling, and ability to reflect systemic physiological changes. In addition to its role in maintaining oral homeostasis, saliva contains a broad spectrum of biomolecules, including proteins, enzymes, hormones, metabolites, and nucleic acids, many of which originate from the systemic circulation. Consequently, alterations

in salivary composition may serve as indicators of underlying systemic disorders. [1,2]

In this review, we focus on various salivary biomarkers found in various systemic diseases like Diabetes Mellitus, Acute Myocardial Infarction, Covid-19 and Mumps.

Diabetes Mellitus

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia arising from defects in insulin secretion, insulin action, or both. It is characterised by polyuria, polydipsia, polyphagia, loss of weight. The global burden of DM continues to rise, and traditional monitoring methods — including capillary blood glucose (fasting and post-prandial) and glycated haemoglobin (HbA1c) — remain invasive and resource-intensive. In recent years, salivary diagnostics has gained attention as a non-invasive, cost-effective, and accessible alternative for screening, monitoring, and potentially early diagnosis of DM. [3,4]

Saliva reflects systemic physiological states as many blood components enter the oral fluid via passive diffusion, active transport, or ultrafiltration. Consequently, numerous analytes detectable in blood, including proteins, metabolites, enzymes, and inflammatory mediators, can be measured in saliva. [3,5]

There are various salivary biomarkers like that of glycemic biomarkers, oxidative Stress and antioxidant biomarkers, inflammatory and immune based biomarkers, proteomic biomarkers and microbiome-based biomarkers.

- **Glycemic Biomarkers**: Elevated salivary glucose levels have been consistently reported in individuals with diabetes compared to healthy controls, mirroring systemic hyperglycemia. Salivary glucose levels correlate positively with fasting and postprandial blood glucose and with HbA1c, suggesting its utility as an adjunctive marker for glycemic status.[6,7] Beyond glucose, studies have identified other carbohydrate-related metabolites in saliva, such as α-hydroxybutyrate and other carbohydrate signatures, which differ significantly between diabetic and non-diabetic individuals. These metabolic changes reflect underlying systemic dysregulation and may enrich diagnostic panels beyond glucose alone.[3]
- **Oxidative Stress and Antioxidant Biomarkers**: Diabetes is associated with increased oxidative stress due to chronic hyperglycemia, resulting in lipid peroxidation and redox imbalance. Several studies have explored salivary antioxidant defense components such as uric acid, glutathione (GSH), catalase, and total antioxidant capacity. In type 2 diabetes mellitus (T2DM), salivary uric acid and GSH were elevated while total antioxidant activity and catalase were reduced compared with healthy controls. [5]
- **Inflammatory and Immune Biomarkers:** Inflammation is a central feature of DM pathophysiology. Salivary inflammatory mediators such as C-reactive protein (CRP), Interleukin-6 (IL-6), and Tumor Necrosis Factor-α (TNF-α) are elevated in individuals with diabetes and show correlations with glycemic control.[8,9] CRP and IL-6, in particular, have shown diagnostic potential in some exploratory analyses.[10] Elevated salivary concentrations of IL-1β and matrix metalloproteinase-8 (MMP-8) correlate with periodontal disease severity in diabetic subjects, although these markers may reflect both systemic inflammation and oral pathology.[11] Additionally, immunoglobulin levels, such as IgA, may be altered in DM, with some evidence of reduced salivary IgA

in type 1 DM, indicating perturbed mucosal immunity.[12]

- **Proteomic Biomarkers**: Recent proteomics studies leveraging liquid chromatography–mass spectrometry (LC-MS/MS) have expanded the repertoire of salivary biomarkers. Functional analysis highlighted immune response and calcium signaling pathways as significantly affected, with candidate proteins such as CAMK2D and SPRR2A correlating with blood glucose and HbA1c levels.[13]
- **Microbiome-Based Biomarkers**: Alterations in the salivary microbiome have been associated with diabetic patients. It is seen that specific taxa like Slackia, Mitsuokella, and Abiotrophia were enriched in diabetic saliva. Thus, a diagnostic model based on microbial profiles achieved promising auxiliary diagnostic performance, indicating the oral microbiome's potential contribution to non-invasive diabetes diagnostics.[14] Additional salivary markers investigated include 1,5-anhydroglucitol, adipokines (e.g., resistin), and stress-related markers such as cortisol and melatonin which require further validation to be used as a diagnostic tool in detecting hyperglycemic from salivary samples.[15]

Acute Myocardial Infarction

Acute myocardial infarction (AMI) remains a leading cause of death globally despite advances in diagnostic and therapeutic strategies. This disease is characterised by presence of intense retrosternal pain which starts at rest, persist longer and not relived by coronary dilators, along with breathlessness, restlessness, increased respiration rate and presence of cyanosis. Early diagnosis is essential for prompt reperfusion therapy and improved patient outcomes. Currently, AMI diagnosis is based on clinical symptoms, electrocardiographic changes, and elevation of serum cardiac biomarkers, particularly cardiac troponins, which are considered the gold standard for myocardial injury detection. [16,17]

However, venous blood sampling is invasive, requires trained personnel, and may limit rapid testing in prehospital or emergency scenarios. Consequently, interest has grown in alternative diagnostic biofluids. Saliva has gained increasing recognition as a diagnostic medium due to its non-invasive collection, minimal risk of infection, patient acceptability, and potential for repeated sampling. [18]

Recent studies have explored the presence and diagnostic relevance of salivary biomarkers in AMI, suggesting that saliva may serve as an adjunct or preliminary screening tool. There are various salivary biomarkers for MI like that of cardiac troponins, C-Reactive Protein, Creatine Kinase-MB and Myoglobin and inflammatory and immune-related biomarkers.

- **Cardiac Troponins**: Cardiac Troponin I (cTnI) and cardiac Troponin T (cTnT) are highly specific markers of myocardial injury. Several studies have demonstrated detectable levels of salivary troponin I in patients with AMI, with significantly higher concentrations compared to healthy controls.[19,20] Although salivary troponin levels are lower than serum concentrations, positive correlations between saliva and serum levels have been reported, suggesting diagnostic relevance.[21]
- **C-reactive protein (CRP)**: It is a well-established inflammatory marker and predictor of adverse cardiovascular events. Elevated salivary CRP levels have been consistently observed in patients with AMI and have shown good discriminatory ability between AMI patients and controls. Salivary CRP may reflect both myocardial injury-associated inflammation and systemic inflammatory status. [19,22]

- **Creatine kinase-MB (CK-MB) and Myoglobin**: They are early markers of myocardial injury in serum. Studies have reported increased salivary CK-MB and myoglobin levels in AMI patients, although findings are less consistent compared to troponins and CRP. Variability in salivary flow rate and assay sensitivity may influence detection. [23]
- **Inflammatory and Immune-Related biomarkers**: Several inflammatory and immune mediators have been investigated in saliva, including matrix metalloproteinase-9 (MMP-9), myeloperoxidase (MPO), soluble CD40 ligand, interleukins, and macrophage inflammatory protein-1α (MIP-1α). These markers are involved in plaque instability, inflammation, and tissue remodelling and have demonstrated altered salivary levels in AMI patients.[24,25]

COVID-19

COVID-19, caused by the novel SARS-CoV-2 virus, rapidly evolved into a global pandemic, affecting millions of individuals worldwide. Early and accurate detection of infection is essential to limit viral transmission and initiate timely treatment. The standard diagnostic method for COVID-19 is detection of viral RNA using reverse transcription polymerase chain reaction (RT-PCR) from nasopharyngeal or oropharyngeal swabs. However, these procedures can be uncomfortable for patients and require trained healthcare personnel for specimen collection. [26]

There are various biomarkers for a patient suffering from covid like viral RNA, salivary antibodies, inflammatory cytokines, oxidative stress markers, metabolomic and proteomic biomarkers.

- **Viral RNA as a salivary biomarker:** The presence of SARS-CoV-2 RNA in saliva is one of the most widely studied biomarkers for COVID-19 diagnosis Studies have demonstrated that saliva samples can contain detectable viral RNA even in asymptomatic or presymptomatic individuals. Viral particles may reach saliva through several mechanisms, including direct infection of salivary gland tissues, contamination from respiratory secretions, and gingival crevicular fluid. [27,28] Saliva-based RT-PCR testing has shown sensitivity comparable to nasopharyngeal swabs in many studies. Additionally, saliva collection reduces exposure risk to healthcare workers and eliminates the discomfort associated with swab collection. [29]
- **Salivary Antibodies:** The immune response to SARS-CoV-2 infection leads to the production of specific antibodies that can be detected in saliva. Salivary immunoglobulins such as IgA, IgG, and IgM against SARS-CoV-2 antigens have been identified in infected individuals. [30]
- **Inflammatory Cytokines:** COVID-19 is characterized by a strong inflammatory response, often referred to as a "cytokine storm." Elevated levels of pro-inflammatory cytokines have been observed in both serum and saliva of infected individuals. Salivary biomarkers such as interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ) have been reported to increase during SARS-CoV-2 infection. These inflammatory markers may provide valuable information regarding disease severity and immune response. [31,32]
- **Oxidative Stress Markers:** Oxidative stress plays a significant role in the pathogenesis of COVID-19. Infection with SARS-CoV-2 can lead to increased production of reactive oxygen species (ROS), resulting in cellular damage and inflammation. Several oxidative stress markers have been identified

in saliva, including malondialdehyde (MDA), total antioxidant capacity (TAC), and glutathione levels. Alterations in these biomarkers may reflect systemic oxidative stress associated with COVID-19 infection and could potentially serve as indicators of disease severity.[33,34]

- **Metabolomic and Proteomic Biomarkers:** Advances in omics technologies have enabled the identification of various salivary metabolites and proteins associated with COVID-19. Proteomic analyses have revealed changes in salivary proteins involved in immune response, inflammation, and cellular metabolism. Metabolomic studies have also identified alterations in amino acids, lipids, and other metabolites in saliva of COVID-19 patients. These changes may provide insights into the metabolic alterations induced by SARS-CoV-2 infection and could serve as potential diagnostic or prognostic biomarkers.[35,36]

MUMPS

Mumps is a contagious viral disease caused by a single-stranded RNA virus of the Paramyxoviridae family, primarily affecting the salivary glands.[37] The hallmark clinical feature is parotitis, characterized by swelling and tenderness of the parotid glands. [38]

The virus is transmitted through respiratory droplets and direct contact with saliva, making saliva both a vehicle for transmission and a valuable diagnostic medium. Viral replication occurs in the upper respiratory tract and spreads to salivary glands, where it induces inflammation and glandular dysfunction.[39,40]

The various salivary biomarkers for an individual suffering from mumps are:

- **Viral RNA as a Salivary Biomarker:** Detection of mumps viral RNA in saliva is the most reliable diagnostic marker. Reverse transcriptase polymerase chain reaction (RT-PCR) performed on buccal or salivary swabs is considered the gold standard for confirmation of infection.[40] Viral RNA can be detected in saliva from several days before to several days after the onset of parotitis, making it useful for early diagnosis.[38] The sensitivity of RT-PCR is highest when samples are collected within the first 3–5 days of symptom onset.[40]
- **Salivary Antibodies:** Salivary immunoglobulins are important biomarkers for mumps diagnosis. Virus-specific IgM antibodies can be detected in saliva during the acute phase of infection, with detection rates up to 75% in early disease and increasing to nearly 100% in later stages.[41] IgG antibodies may also be detected in saliva, indicating past infection or immune response; however, their diagnostic sensitivity is lower compared to IgM in acute infection. [42]
- **Inflammatory Markers:** Saliva reflects the host immune response to infection. Elevated levels of cytokines, enzymes, and inflammatory mediators may be present during mumps infection, reflecting glandular inflammation. [42]

Conclusion

Salivary biomarkers have emerged as a promising and innovative approach in the field of diagnostic medicine. Saliva, as a readily accessible and non-invasive biofluid, contains a wide range of biomolecules including proteins, enzymes, hormones, antibodies, metabolites, and nucleic acids that reflect both oral and systemic states. Advances in molecular biology, proteomics, genomics, and biosensor technologies have enabled the identification and quantification of these biomarkers, making saliva a valuable alternative to blood-based diagnostics. The ability to detect disease-related molecules in saliva offers significant advantages including ease of collection,

reduced patient discomfort, minimal risk of infection transmission, and suitability for repeated sampling and large-scale screening. Despite these advantages, certain challenges remain, including variability in salivary composition, the need for standardized collection and processing protocols, and the requirement for highly sensitive analytical techniques to detect low-concentration biomarkers. Continued research and technological advancements are therefore essential to improve the sensitivity, specificity, and clinical reliability of salivary diagnostic tests. With further validation and standardization, saliva-based diagnostic platforms have the potential to become an integral component of personalized medicine, enabling early disease detection, improved patient monitoring, and more accessible healthcare solutions.

References

1. Wong DT. Salivaomics. The Journal of the American Dental Association. 2012 Oct 1;143:19S-24S.
2. Javaid MA, Ahmed AS, Durand R, Tran SD. Saliva as a diagnostic tool for oral and systemic diseases. Journal of oral biology and craniofacial research. 2016 Jan 1;6(1):67-76.
3. Srinivasan M, Blackburn C, Mohamed M, Sivagami AV, Blum J. Literature-based discovery of salivary biomarkers for type 2 diabetes mellitus. Biomark Insights. 2015;10:39–45. doi:10.4137/BMI.S22177.
4. Cenzato N, Cazzaniga F, Maspero C, Tartaglia GM, Del Fabbro M. Saliva-based diagnostic approach for diabetes mellitus: a step towards non-invasive detection – a scoping review. Eur Rev Med Pharmacol Sci. 2023;27(24):12080–12087.
5. Mussavira S, Dharmalingam M, Sukumaran BO. Salivary glucose and antioxidant defense markers in type II diabetes mellitus. Turk J Med Sci. 2015;45(1):141–147.
6. Calixto PS, Ferraz FC, Dutra GC, et al. Exploring saliva as a sample for non-invasive glycemic monitoring in diabetes: a scoping review. Biomedicines. 2025;13(3):713. doi:10.3390/biomedicines13030713.
7. Baishya R, Lahkar M, Bora M, Mazumdar A. Correlation of salivary glucose level with blood glucose level in diabetes mellitus: a cross-sectional study. Int J Res Med Sci. 2023;11(4):1287–1291.
8. Ladgotra A, Verma P, Sunder Raj S. Estimation of salivary and serum biomarkers in diabetic and non-diabetic patients – a comparative study. J Clin Diagn Res. 2016;10(6):ZC56–ZC60.
9. Zhang Y, Huang Y, Zheng Y, et al. Salivary proteomics of patients with type 2 diabetes identify potential biomarkers for diabetes and highlight significant role of immune response. Clin Exp Med. 2026;26(1):103. doi:10.1007/s10238-025-01203-9.
10. Cui Y, Zhang H, Wang S, et al. Obtaining a reliable diagnostic biomarker for diabetes mellitus by standardizing salivary glucose measurements. Biomolecules. 2022;12(10):1335. doi:10.3390/biom12101335.
11. Takahashi N, Kobayashi D, Nakamura T, et al. Salivary levels of inflammatory cytokines in patients with type 2 diabetes mellitus. J Oral Sci. 2017;59(4):573–580.
12. Preshaw PM, Alba AL, Herrera D, et al. Periodontitis and diabetes: a two-way relationship. Diabetologia. 2012;55(1):21–31.
13. Steigmann L, Maier A, Horvath A, et al. Changes in salivary biomarkers associated with periodontitis and diabetic neuropathy in individuals with type 1 diabetes. Sci Rep. 2022;12:15634. doi:10.1038/s41598-022-19830-5.

14. Long J, Cai Q, Steinwandel M, et al. Association of oral microbiome with type 2 diabetes risk. J Periodontal Res. 2017;52(3):636–643.
15. Goodson JM, Hartman ML, Shi P, et al. Salivary biomarkers for detection of systemic diseases. Clin Oral Investig. 2014;18(3):829–838.
16. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction. Circulation. 2018;138(20):e618-e651.
17. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes. Circulation. 2014;130(25):e344-e426.
18. Wong DT. Salivary diagnostics powered by nanotechnologies, proteomics and genomics. J Am Dent Assoc. 2006;137(3):313-321.
19. Miller CS, Foley JD, Bailey AL, et al. Current developments in salivary diagnostics. Biomark Med. 2010;4(1):171-189.
20. Floriano PN, Christodoulides N, Miller CS, et al. Use of saliva-based nano-biochip tests for acute myocardial infarction at the point of care. Clin Chem. 2009;55(8):1530-1538.
21. Mirzaii-Dizgah I, Riahi E. Salivary troponin I as a novel biomarker for detection of acute myocardial infarction. Dent Res J. 2013;10(4):473-476.
22. Punyadeera C, Dimeski G, Kostner K. Saliva as a tool to assess systemic diseases. Clin Chem Lab Med. 2011;49(6):883-895.
23. Malathi N, Mythili S, Vasanthi HR. Salivary diagnostics: a brief review. ISRN Dent. 2014; 2014:158786.
24. Miller CS, King CP Jr, Langub MC Jr, Kryscio RJ, Bailey AL. Salivary biomarkers of existing periodontal disease: a cross-sectional study. J Am Dent Assoc. 2006;137(3):322-329.
25. Zhang CZ, Cheng XQ, Li JY, et al. Saliva in the diagnosis of diseases. Int J Oral Sci. 2016;8(3):133-137
26. Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in different types of clinical specimens. JAMA. 2020;323(18):1843-4.
27. To KK, Tsang OT, Yip CC, Chan KH, Wu TC, Chan JM, et al. Consistent detection of 2019 novel coronavirus in saliva. Clin Infect Dis. 2020;71(15):841-3.
28. Sabino-Silva R, Jardim ACG, Siqueira WL. Coronavirus COVID-19 impacts to dentistry and potential salivary diagnosis. Clin Oral Investig. 2020;24:1619-21.
29. Wyllie AL, Fournier J, Casanovas-Massana A, Campbell M, Tokuyama M, Vijayakumar P, et al. Saliva or nasopharyngeal swab specimens for detection of SARS-CoV-2. N Engl J Med. 2020;383(13):1283-6.
30. Isho B, Abe KT, Zuo M, Jamal AJ, Rathod B, Wang JH, et al. Evidence for sustained mucosal and systemic antibody responses to SARS-CoV-2. Sci Immunol. 2020;5(52):eabe5511.
31. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with SARS-CoV-2 in Wuhan, China. Lancet. 2020;395(10223):497-506.
32. Chen L, Zhao J, Peng J, Li X, Deng X, Geng Z, Shen Z, Guo F, Zhang Q, Jin Y, Wang L. Detection of SARS-CoV-2 in saliva and characterization of oral symptoms in COVID-19 patients. Cell proliferation. 2020 Dec;53(12):e12923.
33. Cecchini R, Cecchini AL. SARS-CoV-2 infection pathogenesis and oxidative stress. Free Radic Biol Med. 2020;163:13-5.

34. Su H, Xu T, Ganapathy S, Shadfan B, Long M, Huang TH, et al. Salivary biomarkers in COVID-19 diagnosis and monitoring. Oral Dis. 2022;28(Suppl 1):909-18.
35. Messner CB, Demichev V, Wendisch D, Michalick L, White M, Freiwald A, et al. Ultra-high-throughput clinical proteomics reveals classifiers of COVID-19 infection. Cell Syst. 2020;11(1):11-24
36. Shen B, Yi X, Sun Y, Bi X, Du J, Zhang C, et al. Proteomic and metabolomic characterization of COVID-19 patient sera. Cell. 2020;182(1):59-72.
37. Hviid A, Rubin S, Mühlemann K. Mumps. Lancet. 2008;371(9616):932–44.
38. Centers for Disease Control and Prevention (CDC). Mumps: Clinical features. MMWR Recomm Rep. 2012;61(RR-2):1–40.
39. Rubin S, Eckhaus M, Rennick LJ, Bamford CGG, Duprex WP. Molecular biology, pathogenesis and pathology of mumps virus. J Pathol. 2015;235(2):242–52.
40. Stoltz K, Puri S, Curry S. Performance of Mumps PCR and Serologic Testing During a University-Associated Mumps Outbreak in Charleston, SC. Infection Control & Hospital Epidemiology. 2020 Oct;41(S1):s19-.
41. Davis NF, McGuire BB, Mahon JA, Smyth AE, O'Malley KJ, Fitzpatrick JM. The increasing incidence of mumps orchitis: a comprehensive review. BJU Int. 2010;105(8):1060–5.
42. Corstjens PL, Abrams WR, Malamud D. Saliva and viral infections. Periodontology 2000. 2016 Feb;70(1):93-110.