REVIEW PAPER
Volume - 9 | Issue - 8 | August - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# DIAGNOSTIC IMPORTANCE OF SALIVA

Dental Science

**Dr Mutum Sangeeta Devi*** Senior lecturer, Madha Dental College and Hospital, Chennai*Corresponding Author

**Dr Manju J** Senior lecturer, Thai Moogambigai Dental College and Hospital, Chennai

**Dr Rahul B** Senior lecturer, Thai Moogambigai Dental College and Hospital, Chennai

**Dr Vasant M Bhanushali** Private Practitioner, Mumbai

## ABSTRACT

As a non-invasive and safe source, saliva could be a blood replacement in disease diagnosis and prognosis. Saliva can manifest from minor infections to malignancies. It is easy for both patients and clinicians to collect saliva. This article describes the latest advances in saliva-related studies and future benefits in early detection of oral diseases, such as dental caries and periodontal disease, as well as other systemic disorders including malignancy. Specific guidelines and outcomes regarding the future are expected. Salivary diagnostics should be available, along with high-sensitivity and various systemic and oral disease specificity tests.

## KEYWORDS

saliva, diagnosis, non-invasive, malignancy.

## INTRODUCTION

Saliva is regarded as a safe diagnostic fluid that can substitute blood tests to monitor a variety of oral and systemic diseases.[1] Daily saliva production in a healthy person ranges from 0.5-1.5 L, with a flow rate of around 0.5 mL / minute. Lubrication and protection of oral tissues, sensing of taste, buffering capacity and digestion of carbohydrates are some of the essential functions of saliva.[2]. Saliva may be collected with different methods under unstimulated conditions or stimulated conditions.[3,4] Saliva proteins, mRNA, miRNA and metabolites are helpful for diagnostic purposes, as both oral and systemic disorders suggest an increased and reduced rate in saliva. Saliva is generally referred to as a liquid biopsy tool, because it is a non-invasive diagnostic method to treat specific systemic conditions.[5] Saliva is secreted by the salivary glands into the oral cavity and is extremely useful for diagnostic applications.[6]

### Dental Caries

Saliva is often used for calculating the number of oral bacteria in saliva. A higher prevalence of caries and root caries was associated with the rising amount of Streptococcus mutans and lactobacilli in saliva.[7] Low salivary buffering ability is a major risk for dental caries, and is also an indicator of lower saliva secretion. The research suggests that salivary measurements in individuals with high dental caries, such as salivary flow rate, salivary viscosity, salivary pH and salivary buffering capacity were lower. Therefore, salivary analysis is prescribed as part of regular care when treating patients with a significant risk of dental caries. [8]

### Periodontal disease

Elevated levels of aspartate aminotransferase (AST) and alkaline phosphatase have been associated with periodontal diseases. Salivary AST could be used as a diagnostic tool for periodontal disease.[9] Detection in saliva of certain types of bacteria may reflect their presence in the dental plaque and in the periodontal pocket. Also, saliva can be used for periodontal diagnosis, due largely to gingival crevicular fluid contributions.[10]

### Orofacial Pain

Orofacial pain is a sensory feeling within a particular area of the anatomy and can be linked to certain common orofacial chronic entities.[11] Also saliva can be used as a measure of stress as well as chronic pain. Many studies have identified substance P, a neuropeptide connected with inflammation and pain, and also the stress hormone cortisol, and markers of oxidative stress within salivary secretions can be identified repeatedly.[12,13]. Glutamate was mainly expressed in whole-stimulated saliva and was also found to be increased under different pain conditions [14]. These findings indicate that glutamate in peripheral tissue may be an effective pain mediator and may therefore serve as a possible biomarker of pain, among others. In conditions of psychological stress there is a rise in the level of salivary amylase and a reduction in the levels of secretory IgA.[15]

### Fungal Infections

Salivary diagnostic tests can be used to identify oral fungi. The study of the salivary fungal count provides useful knowledge in oral candidiasis cases. In such cases, changes in salivary proteins, such as immunoglobulins, Hsp70, calprotectin, histatins, mucins, simple proline rich proteins and peroxidases also have a significant diagnostic value. [16,17]

### Viral infections

In saliva, antibodies against viruses as well as viral components can also be detected and can help diagnose acute viral infections, congenital infections and reactivate infections.[18] The oral mucosal transudate that is obtained by swabbing the mouth and tongue contains a combination of sIgA, IgG, IgM and a high content of antibodies [11]. The measles virus basic IgM was found in saliva in a test carried out by Oliveira et al.[19]Salivary IgA levels drop to HIV with patients getting symptomatic.[20] Hepatitis Saliva has been found to be a beneficial serum substitute for the diagnosis of viral hepatitis. Diagnosis of acute hepatitis A (HAV) and hepatitis B (HBV) based on the existence of IgM antibodies in saliva. DNA of hepatitis B virus discovered in saliva by polymerase chain reaction. [21]

### Bacterial Infections

Saliva is used to diagnose infection with Helicobacter Pylori which is the main pathogen associated in peptic ulcer.[22] H. Pylori saliva antibodies can be useful in predicting gastric adenocarcinoma risk factor.

### Sjogren's Syndrome

Sjogren syndrome (SS) is an autoimmune disorder characterized by reduce salivary and lacrimal gland secretion, and associated endocrine disorder. An increase in immunoglobulin levels, inflammatory mediators, albumin, sodium and chloride and a decrease in phosphate level are indicative of SS.[1,23] Serum chemistry can show polyclonal hypergammaglobulinemia and high rheumatoid factor, anti-SS-B antibody, antinuclear antibody and anti-SS-A. Also, the saliva of patients with SS reported increased concentrations of sodium and chloride, lacoferrin, IgA, IgG, and albumin, and a decreased concentration of phosphate. Increased salivary concentrations of inflammatory mediators has also been reported. Also increase levels of salivary soluble interleukin-2 receptor were also reported in patient with SS. [24,25]

### Cystic fibrosis

Cystic fibrosis (CF), a most common genetic disorder in Caucasians, is an inherited exocrinopathy with a broad range of clinical and genetic variants.[26] Alteration of ion concentration seen in sweat and saliva in CF.[27] In CF patients, salivary calcium, magnesium concentration and lactate dehydrogenase levels were raised when compared with healthy controls [2,28] Most research suggests high levels of calcium and proteins in CF patients with submandibular saliva and result in an aggregation of calcium-proteins that triggered saliva turbidity.[29-32]

### Diabetes mellitus

Diabetes is a metabolic condition resulting from inadequate insulin production, insulin action or resistance to insulin, resulting in a disorder of glucose metabolism. A positive association was found among α-2-macroglobulin and HbA1c, which suggested that in patients with type 2 diabetes mellitus, α-2-macroglobulin levels in the saliva may indicate glycaemic regulation.[33] There was a positive correlation between concentrations of both HbA1c and salivary glucose, and diabetes patients. In patients with diabetes mellitus, this suggested that the blood glucose concentration can be monitored by saliva.[34]

### Cardiovascular disease

Cardiovascular disease (CVD) is connected to the circulatory system which involves atherosclerosis, cardiac attack which myocardial infarction. The levels of α-2-HS-glycoprotein in saliva have reduced in CVD patients, suggesting that the peptidome may provide a possible means for early detection of CVD patients.[35] Acute myocardial infarction can be detected as salivary cardiac troponin (cTn) levels rise and/or fall. CTn in the saliva may be used to identify acute myocardial infarction, but is poorly diagnosed.[36]

### Monitoring of Drugs

A variety of saliva-based drugs can be easily tracked. Saliva can also be used to track patient adherence to psychiatric medicines. Also, saliva is useful in assessing anti-epileptic drugs and anti-cancer medications. There are other many drugs that can be found in saliva[37-39]

### Malignancy

Saliva is being used as a diagnostic tool for oral squamous cell carcinoma (OSCC), and in its diagnosis salivary analytes such as proteins, mRNA, and DNA are being used. Long non-coding, aberrant expressions of RNA (lncRNA) are connected with lung, breast as well as prostate carcinomas. Tang et al. found, in their study, that saliva contained a detectable amount of lncRNA that could be potential OSCC markers.[40] Inactive p53 protein accumulation occurs which in turn contributes to the development of antibodies directed against this p53 protein. In patients diagnosed with oral squamous cell carcinoma (SCC), the p53 antibodies can also be found in the saliva and can thus help in early detection and monitoring for this tumor.[41]

### Forensic science

Another common use in forensic science is salivary analyses. Removing saliva, whether directly from either a suspect or from the victim's injury, can facilitate DNA analysis. The cotton swabs can be used for gathering a saliva sample. An amylase assay kit can be used to examine the dried saliva from bite wounds which patient has suffered.[42] It is easy to obtain the salivary samples from envelopes, bottles, food products cigarettes, as well as other sources. A vast number of patients secrete blood group antigens into their saliva that can be used to identify perpetrators and prosecute paternity law suits.[43]

## CONCLUSION

Saliva is a biofluid that is potentially rich in diagnostic markers for oral as well as systemic diseases. Several methodologies have developed in recent decades for determining the microbial as well as molecular constituency of saliva. Saliva is generally considered our body's mirror. It is useful as it is non-invasive, easy collection, readily accessible and cost-effective in contrast to other diagnostic approaches.

Financial Support and Sponsorship
Nil.

Conflicts of Interest
There are no conflicts of interest.

## REFERENCE

1. Malamud D (2011) Saliva as a diagnostic fluid. Dent Clin North Am 55: 159- 178
2. Pfaffe T, Cooper-White J, Beyerlein P, Kostner K, Punyadeera C. Diagnostic potential of saliva: current state and future applications. Clin Chem 2011; 57:675-87.
3. Miller CS, Foley JD, Bailey AL, Campell CL, Humphries RL, Christodoulides N, et al. Current developments in salivary diagnostics. Biomark Med 2010; 4:171-89.
4. Navazesh M. Methods for collecting saliva. Ann N Y Acad Sci 1993; 694:72-7.
5. Aro K, Wei F, Wong DT, Tu M. Saliva Liquid Biopsy for Point-of-Care Applications. journal.frontiersin.org/article/10.3389/fpubh.2017.00077/
6. Wong DTW. Salivary Diagnostics: Scientific and Clinical Frontiers. Wong DTW, editor. Adv Dent Res. 2011 Oct;23(4):350–2.
7. S. Mittal, V. Bansal, S. Garg, G. Atreja, and S. Bansal, "The diagnostic role of Saliva—a review," Journal of Clinical and Experimental Dentistry, vol. 3, no. 4, pp. e314–e320, 2011.
8. Van Nieuw Amerongen A, Bolscher JG, Veerman EC. Salivary proteins: protective and diagnostic value in cariology? Caries Res. 2004; 38:247-53.
9. A. Totan, M. Greabu, C. Totan, and T. Spinu, "Salivary aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase: possible markers in periodontal diseases?" Clinical Chemistry and Laboratory Medicine, vol. 44, no. 5, pp. 612–615,2006.
10. Asikainen S, Alaluusua S, Saxen L (1991). Recovery of Actinomycetemocomitans from teeth, tongue, and saliva. J Periodontol 62:203-206.
11. J. P. Goulet and A. M. Velly, Orofacial Pain Biomarkers, Springer, 2017.
12. H. Merskey and N. Bugduk, Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms, ASP Task Force on Taxonomy, Ed., IASP Press, Seattle, WA, USA, 2nd edition, 1994.
13. R. De Leeuw and G. D. Klasser, Orofacial Pain – Guidelines for Assessment, Diagnosis, and Management, Quintessence, Chicago, IL, USA, 5th edition, 2013.
14. H. Jasim, A. Carlsson, B. Hedenberg-Magnusson, B. Ghafouri, and M. Ernberg, "Saliva as a medium to detect and measure biomarkers related to pain," Scientific Reports, vol. 8, no. 1, pp. 3220–3229, 2018. [98]
15. A. Shimada, E. E. Castrillon, L. Baad-Hansen et al., "Increased pain and muscle glutamate concentration after single ingestion of monosodium glutamate by myofascial temporomandibular disorders patients," European Journal of Pain, vol. 20, no. 9, pp. 1502–1512, 2016.
16. O. J. Bergmann, "The demonstration of candidal pseudohyphae in salivary smears as a method of early diagnosis of oral candidiasis in patients with acute myeloid leukemia," Oral Microbiology and Immunology, vol. 11, no. 5, pp. 362–364, 1996.View at:
17. G. Liguori, A. Lucariello, G. Colella, A. de Luca, and P. Marinelli, "Rapid identification of Candida species in oral rinse solutions by PCR," Journal of Clinical Pathology, vol. 60, no. 9, pp. 1035–1039, 2007.View at:
18. Mortimer PP, Parry JV (1988). The use of saliva for viral diagnosis and screening. Epidemiol Infect 101:197-201
19. S. A. Oliveira, M. M. Siqueira, D. W. G. Brown, L. A. B. Camacho, T. Faillace, and B. J. Cohen, "Salivary diagnosis of measles for surveillance: A clinic-based study in Niteroi, state of Rio de Janeiro, Brazil," Transactions of the Royal Society of Tropical Medicine and Hygiene, vol. 92, no. 6, pp. 636–638, 1998.
20. Malamud D. Oral diagnostic testing for detecting human immunodeficiency virus-1 antibodies: a technology whose time has come. Am J Med. 1997; 102:9–14.
21. Oba IT, Spina AM, Saraceni CP, Lemos MF, Senhoras R, Moreira RC, et al. detection of hepatitis A antibodies by ELISA using saliva as clinical samples. Rev Inst Med Trop Sao Paulo. 2000; 42:197- 200.
22. Kountorar (1988); Diagnostic test for Helicobacter pyroli; Gut 42:900-901.
23. M. Greabu, M. Battino, M. Mohora et al., "Saliva—a diagnostic window to the body, both in health and in disease," Journal of Medicine and Life, vol. 2, no. 2, pp. 124–132, 2009.
24. Nihon Rinsho Meneki Gakkai Kaishi, anti-SS-A/Ro and anti-SS-B/La antibodies of IgA and IgG isotypes in saliva and sera of patients with Sjogren's syndrome. 2003; 26:346-54.
25. Fox RI, Kang HI (1992). Pathogenesis of Sjögren's syndrome. Rheum Dis Clin North Am 18:517-538.
26. Vining RF, McGinley RA (1986). Hormones in saliva. Crit Rev ClinLab Sci 23:95-146.
27. Straus Baugh SD, Davis PB: Cystic fibrosis: a review of epidemiology and pathobiology. Clin Chest Med 2007, 28(2):279–288.
28. A. C. Gonc¸alves, F. A. Marson, R.M. Mendonc¸a et al., "Saliva as a potential tool for cystic fibrosis diagnosis," Diagnostic Pathology, vol. 8, p. 46, 2013.
29. Mandel ID, Kutscher A, Denning CR, Thompson RH (1967). Salivary studies in cystic fibrosis. Am J Dis Child 110:431-438.
30. Blomfield J, Rush AR, Allars HM, Brown JM (1976). Parotid gland function in children with cystic fibrosis and child control subjects. Pediatr Res 10:574-578.
31. Mangos JA, Donnelly WH (1981). Isolated parotid acinar cells from patients with cystic fibrosis. Morphology and composition. J Dent Res 60:19-25.
32. Boat TF, Weisman UN, Pallavicini JC (1974). Purification and properties of the calcium precipitable protein in submaxillary saliva of normal and cystic fibrosis subjects. Pediatr Res 8:531- 534.
33. Aitken JP, Ortiz C, Morales-Bozo I et al. α-2-macroglobulin in saliva is associated with glycemic control in patients with type 2 diabetes mellitus. Dis Markers 2015: 128653.
34. Satish BN, Srikala P, Maharudrappa B et al. Saliva: a tool in assessing glucose levels in diabetes mellitus. J Int Oral Health 2014; 6(2): 114–117.
35. Zheng H, Li R, Zhang J et al. Salivary biomarkers indicate obstructive sleep apnea patients with cardiovascular diseases. Sci Rep 2014; 4: 7046.
36. Floriano PN, Christodoulides N, Miller CS, Ebersole JL, Spertus J, Rose BG, et al. Use of saliva-based nano-biochip tests for acute myocardial infarction at the point of care: A feasibility study. Clin Chem 2009; 55:1530-8.
37. Rai B, Kharb S, Anand SC. Saliva as a Diagnostic Tool in Medical Science: A Review Study. Advances in Medical and Dental Sciences 2008;2(9): 9-12
38. Cone EJ, Huestis MA. Interpretation of oral fluid tests for drugs of abuse. Saliva testing for drugs of abuse. Ann NY Acad Sci. 2007; 1098:51–103.
39. Vasudev A, Tripathi KD, Puri V. Correlation of serum and salivary carbamazepine concentration in epileptic patients: implications for therapeutic drug monitoring. Neurol India. 2002; 50:60-2.
40. H. Tang, Z. Wu, J. Zhang, and B. Su Salivary, "lncRNA as a potential marker for oral squamous cell carcinoma diagnosis," Molecular Medicine Reports, vol. 7, no. 3, pp. 761–766, 2013.
41. Warnakulasuriya S, Soussi T, Maher R, Johnson N, Tavassoli M. Expression of p53 in oral squamous cell carcinoma is associated with the presence of IgG and IgA p53 autoantibodies in sera and saliva of the patients. J Pathol. 2000; 192:52-7.
42. Aps JK, Martens LC. Review: The physiology of saliva and transfer of drugs into saliva. Forensic Sci Int. 2005; 150:119-31.
43. D. Sweet and D. Hildebrand, "Saliva from cheese bite yields DNA profile of burglar: a case report," International Journal of Legal Medicine, vol. 112, no. 3, pp. 201–203, 1999.