

## Saliva- A Diagnostic Tool

Dr Vijaylaxmi B Madalli, Dr Shrinivas M Basavaraddi, Dr Krishna Burde,  
Dr Priya Horatti

Assistant professor, Department of Oral medicine and radiology, SDM College of Dental Sciences, Sattur,  
Dharwad, Karnataka India-580009.

Reader, Department of Orthodontics, SDM College of Dental Sciences, Sattur, Dharwad, Karnataka India-  
580009.

Professor and Head, Department of Oral medicine and radiology, SDM College of Dental Sciences, Sattur,  
Dharwad, Karnataka India-580009

Professor and Head, Department of General Dentistry, SDM College of Dental Sciences, Sattur, Dharwad,  
Karnataka India-580009

---

**Abstract:** Saliva as a diagnostic fluid offers distinctive advantages over serum because it can be collected non-invasively by individuals with modest training. Furthermore, saliva may provide a cost-effective approach for the screening of large populations. Whole saliva may be used for diagnosis of systemic diseases, because it contains serum constituents. This review explains the diagnostic application of saliva for hereditary disorders, autoimmune diseases, malignant and infectious diseases, and endocrine disorders, as well as in the assessment of therapeutic levels of drugs and the monitoring of illicit drug use, and also for forensic evidence and others. In future we are likely to see the increased utilization of saliva as a diagnostic fluid. As we enter the era of genomic medicine, sialochemistry will play an increasingly important role in the early detection, the monitoring and progression of the systemic and oral diseases.

**Key words:** Saliva, Sialochemistry, Caries, Disease, Diagnosis.

---

### I. Introduction

The analysis of blood, the most frequent specimen in clinical chemistry, has two purposes: first, to identify individuals with disease and second, to follow the progress of the affected individual under medical treatment. A similar use has been envisioned for salivary secretions.<sup>1</sup> The diagnostic use of saliva has attracted the attention of numerous investigators because of the noninvasive nature and relative simplicity of collection.<sup>1</sup> Saliva is not one of the popular bodily fluids. It lacks the drama of blood, the sincerity of sweat and the emotional appeal of tears. Despite the absence of charisma, a growing number of internists, pediatricians, pharmacologists, clinical and forensic pathologists, endocrinologists, immunologists, psychologists and dentists are finding that saliva provides an easily available, noninvasive diagnostic medium for a rapidly widening range of diseases and clinical situations.<sup>2</sup> The clinical applications of saliva range from the forensic field to drug monitoring and diagnosis of systemic and local conditions.

Saliva is the product of multiple salivary glands lying beneath the oral mucosa. Each day, the human salivary glands produce almost 600 mL of serous and mucinous saliva containing minerals, electrolytes, buffers, enzymes and enzyme inhibitors, growth factors and cytokines, immunoglobulins (e.g., secretory immunoglobulin A [IgA]), mucins and other glycoproteins.<sup>3</sup>

### II. Advantages Of Saliva As A Diagnostic Fluid<sup>4,5</sup>

1. Noninvasive diagnosis of disease and monitoring of general health.
2. Painless, patient suffers no discomfort and little anxiety in the collection process.
3. Simple in collection with a modest trained assistant and applicable in remote areas.
4. Relatively cheap technology as compared to other tests.
5. Cost effective applicability for screening large population.
6. Can be used to study special population where blood sampling is a problem e.g children, anxious /handicap/ elderly patients.
7. Convenient for multisampling.
8. Safer for health professionals than blood tests.
9. Compared to blood and urine, saliva is also cheaper to store and ship.
10. In addition saliva does not clot and can be manipulated more easily than blood.

### III. Limitations<sup>5,6</sup>

1. Levels of certain markers in saliva are not always a reliable reflection of the levels of these markers in serum.
2. Salivary composition can be influenced by the method of collection and degree of stimulation of salivary flow.
3. Changes in salivary flow rate may affect the concentration of salivary markers and also their availability due to changes in salivary pH.
4. Variability in salivary flow rate is expected between individuals and in the same individual under different conditions.
5. In addition, many serum markers can reach whole saliva in an unpredictable way (*i.e.* gingival crevicular fluid flow and through oral wounds). These parameters will affect the diagnostic usefulness of many salivary constituents.
6. Furthermore, certain systemic disorders, numerous medications and radiation may affect salivary gland function and consequently the quantity and composition of saliva.
7. Whole saliva also contains proteolytic enzymes derived from the host and from oral microorganisms. These enzymes can affect the stability of certain diagnostic markers. Some molecules are also degraded during intracellular diffusion into saliva.

Analysis of saliva done for the diagnosis of following -<sup>7</sup>

1. Hereditary disease
2. Autoimmune disease
3. Malignancy
4. Infection
5. Monitoring of levels of hormones
6. Monitoring of levels of drugs.
7. Bone turnover marker in saliva
8. Forensic Evidence
9. Dental caries and periodontal disease
10. Diagnosis of Oral Disease with Relevance for Systemic Diseases

#### 1. Hereditary diseases

Cystic fibrosis (CF) is a genetically transmitted disease of children and young adults. Elevations in electrolytes (sodium, chloride, calcium, and phosphorus), urea and uric acid, total protein and lipid were observed in the submandibular saliva of CF patients.<sup>8</sup>

21-Hydroxylase deficiency is an inherited disorder of steroidogenesis which leads to congenital adrenal hyperplasia. Early morning salivary levels of 17-hydroxyprogesterone (17-OHP) determined by ELISA is an excellent screening test for the diagnosis of non-classic 21-hydroxylase deficiency, since the salivary levels accurately reflected serum levels of 17-OHP.<sup>9</sup>

#### 2. Autoimmune diseases

Sjögren's syndrome Serum chemistry can demonstrate polyclonal hypergammaglobulinemia and elevated levels of rheumatoid factor, antinuclear antibody, anti-SS-A, and anti-SS-B antibody. In addition, increased concentrations of sodium and chloride, IgA, IgG, lactoferrin, and albumin, and a decreased concentration of phosphate were reported in saliva of patients with SS.<sup>10</sup>

#### 3. Malignancy

The mRNA levels for specific proteins are elevated in the saliva of head and neck cancer patients. The p53 antibodies can be detected in the saliva of patients diagnosed with oral squamous cell carcinoma (SCC), and can thus assist in the early detection and screening for, this tumor. Elevated levels of salivary defensin-1 were found to be indicative of the presence of oral SCC. CA 125 is a tumor marker for cancer. Elevated salivary levels of CA 125 were detected in patients with untreated breast cancer than healthy controls and patients who were treated for breast cancer.<sup>11</sup>

#### 4. Infectious diseases

There was considerable variation in the detection rate of *H.pylori* DNA in salivary samples.<sup>12</sup> In the children infected with Shigella revealed higher titers of anti-Shiga toxin antibody in comparison with healthy controls.<sup>13</sup> Reactivation of herpes simplex virus type-1 (HSV-1) is involved in the pathogenesis of Bell's palsy and PCR based identification of virus DNA in saliva is a useful method for the early detection of HSV-1 reactivation in patients with Bell's palsy.<sup>14</sup> Dengue is a mosquito-transmitted viral disease. Salivary levels of anti-dengue IgM and IgG demonstrated sensitivity of 92% and specificity of 100% in the diagnosis of infection.<sup>15</sup>

### **5. Detection of drugs**

Saliva has been proposed for the monitoring of systemic levels of drugs. Saliva may be used for monitoring patient compliance with psychiatric medications. Saliva is also useful for the monitoring of anti-epileptic drugs and anti-cancer drugs. Estimation of salivary carbamazepine levels is predictable and convenient method of drug monitoring in epileptic patient, and a positive correlation ( $r = 0.659$ ) between salivary and serum carbamazepine levels was observed.<sup>16</sup> Other recreational drugs that can be identified in saliva are amphetamines, barbiturates, benzodiazepines, cocaine, phencyclidine (PCP), and opioids.<sup>17</sup> Nicotine saliva can be used to monitor tobacco smoking and exposure to tobacco smoke. The major nicotine metabolite nicotine was investigated as an indicator of exposure to tobacco smoking. Monitoring level of salivary cotinine has proven useful in monitoring compliance with smoking cessation programs.<sup>18</sup>

### **6. The Monitoring of Hormone Levels**

Saliva can be analyzed as part of the evaluation of endocrine function. Cortisol due to their lipid solubility, steroid hormones can be detected in saliva Salivary aldosterone correlated significantly to plasma aldosterone levels ( $r = 0.60$ ), and increased aldosterone levels were found in both the serum and saliva of patients with primary aldosteronism (Conn's syndrome).<sup>19</sup> Progesterone - Salivary progesterone levels showed good correlation with free serum levels. Elevated salivary estradiol is associated with increased risk of preterm birth.<sup>20</sup> Insulin - Insulin can be detected in saliva, a positive correlation between saliva and serum insulin levels following a glucose tolerance test was reported for healthy subjects, diabetic patients.<sup>21</sup> Saliva also contains multiple components whose concentrations are altered by diabetes, some of which (glucose,  $\alpha$ -amylase, and ghrelin) have strong diagnostic potential.<sup>22</sup> Serum and salivary levels of protein hormones are not well-correlated. These hormones are too large to reach saliva by means of passive diffusion across cells or by ultrafiltration, and the detection of these hormones in saliva is primarily due to contamination from serum through GCF or oral wounds.<sup>23</sup>

### **7. Bone Turnover Marker in Saliva**

Saliva can be used to measure bone turnover. Mcgehee and Johnson used commercially available ELISA to test for the presence of osteocalcin (OC) and pyridinoline (PYD) in the whole human saliva of women.<sup>24</sup>

### **8. Forensic Evidence**

Saliva may be found on victims of several violent crimes. Saliva can potentially be recovered from bite marks, cigarette butts, postage stamps, envelopes and other objects.<sup>25</sup>

### **9. Dental Caries and Periodontal Disease**

High numbers of *S. Mutans* and *Lactobacillus* indicate a shift in oral microflora from healthy to more cariogenic. Progress from gingivitis to periodontal disease is determined by genetic susceptibility, and the presence of pathogenic bacteria.<sup>26</sup> People at high risk for periodontal disease can be determined by genetic screening. DNA can easily be isolated from oral epithelial cells, collected by use of a buccal swab, one of the most common oral diagnostics.<sup>27</sup>

### **10. Diagnosis of Oral Disease with Relevance for Systemic Diseases**

Some systemic diseases affect salivary glands directly or indirectly, and may influence the quantity and quality of saliva. Quantitative alterations in saliva may be a result of medications. At least 400 drugs may induce xerostomia.<sup>28</sup> Reduced salivary flows may lead to progressive dental caries, fungal infection, oral pain, and dysphagia.<sup>28</sup> Qualitative changes in salivary composition can also provide diagnostic information concerning oral problems. Increased levels of albumin in whole saliva were detected in patients who received chemotherapy and subsequently developed stomatitis. It is envisioned that with the human salivary proteome available, one can begin to examine and as Sjogren syndrome, osteoporosis, rheumatoid arthritis, diabetes, and cancers.<sup>29</sup>

## **IV. Conclusion:**

Although blood is still the gold standard for diagnostics of diseases and drugs, Saliva offers an alternative to serum as a biologic fluid for diagnostic purposes. The components of saliva act as a "mirror of the body's health," and the widespread use and growing acceptability of saliva as a diagnostic tool is helping individuals, researchers, health care professionals and community health programs to better detect and monitor disease and to improve the general health of the public.

## References:

- [1]. A Aguirre, LA Testa-Weintraub. Sialochemistry: A diagnostic tool? *Crit Rev Oral Biol Med* 1993;4(3/4):343-50.
- [2]. Mandel ID. The diagnostic uses of saliva. *J Oral Pathol Med* 1990;19(3):119-25.
- [3]. Herenia P, Lawrence. Salivary markers of systemic disease: noninvasive diagnosis of disease and monitoring of general health *J Can Dent Assoc* 2002; 68(3):170-4.
- [4]. Malamud D. Salivary diagnostics: The future is now. *J Am Dent Assoc* 2006; 137:284- 286.
- [5]. D K Gupta, V Singh, A Singh, R K Dubey, G B Gupta. Saliva - A non invasive diagnostic tool for aging population. *Journal of the Indian Academy of Geriatrics*, 2011; 7: 177-181.
- [6]. Lee Y, Wong DT. Saliva: an emerging biofluid for early detection of diseases. *Am J Dent* 2009; 22:241-248.
- [7]. Mittal S, Bansal V, Garg S, Atreja G, Bansal S. The diagnostic role of Saliva — A Review. *J Clin Exp Dent*. 2011;3(4):e314-20.
- [8]. Slomiany BL, Aono M, Murty VL, Slomiany A, Levine MJ, Tabak LA. Lipid composition of submandibular saliva from normal and cystic fibrosis individuals. *J Dent Res*.982;61:1163–6.
- [9]. Ueshiba H, Zerah M, new MI. Enzyme-linked immunosorbent assay (ELISA) method for screening of non-classical steroids 21-hydroxylase deficiency. *Horm Metab Res*. 1994;26:43-5.
- [10]. Iwasaki K, Okawa-Takatsuji M, Aotsuka S, Ono T. Detection of 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. *Nihon Rinsho Meneki Gakkai Kaishi*. 2003;26:346-54.
- [11]. 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.
- [12]. Kabir S. Detection of helicobacter pylori DNA in feces and saliva by polymerase chain reaction: a review. *Helicobacter*. 2004;9:115-23.
- [13]. Schultz C, Qadri F, Hossain SA, Ahmed F, Ciznar I. Shigella-specific IgA in saliva of children with bacillary dysentery. *FEMS Microbiol Immunol*. 1992;4:65–72.
- [14]. Lazarini PR, Vianna MF, Alcantara MP, Scalia RA, Caiaffa Filho HH. Herpes simplex virus in the saliva of peripheral Bell's palsy patients. *Braz J Otorhinolaryngol*. 2006;72:7-11.
- [15]. Chakravarti A, Matlani M, Jain M. Immunodiagnosis of dengue virus infection using saliva. *Curr Microbiol*. 2007;55:461-4.
- [16]. 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.
- [17]. 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.
- [18]. Figueiredo VC, Szklo M, Szklo AS, Benowitz N, Lozana JA, Casado L, et al. Determinants of salivary cotinine level: a population based study in Brazil. *Rev Saude Publica*. 2007;41:954-62.
- [19]. Raff H. Utility of salivary cortisol measurements in Cushing's syndrome and adrenal insufficiency. *J Clin Endocrinol Metab*.2009;94:3647-55.
- [20]. Heine RP, McGregor JA, Goodwin TM, Artal R, Hayashi RH, Robertson PA, Varner MW. Serial salivary estriol to detect an increased risk of preterm birth. *Obstet Gynecol*. 2000;96:490-7.
- [21]. Pasic J, Pickup JC. Salivary insulin in normal and type I diabetic subjects. *Diabetes Care*. 1988;11:489–494.
- [22]. Aydin S. A comparison of ghrelin, glucose, alpha-amylase and protein levels in saliva from diabetics. *J Biochem Mol Biol*.2007;40:29-35.
- [23]. Groschl M. Current status of salivary hormone analysis. *Ann Biol Clin (Paris)*. 2009;67:493-504.
- [24]. McGehee JW Jr, Johnson RB. Biomarkers of bone turnover can be assayed from human saliva. *J Gerontol A Biol Sci Med Sci*. 2004;59:196-200.
- [25]. Sweet D, Hildebrand D. Saliva from cheese bite yields DNA profile of burglar: a case report. *Int J Legal Med*. 1999;112:201-3.
- [26]. Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal disease. *Lancet*. 2005;366:1809-20.
- [27]. Morrison HI, Ellison LF, Taylor GW. Periodontal disease and risk of fatal coronary heart and cerebrovascular disease. *J Cardiovasc Risk*. 1999;6:7-11.
- [28]. Rees TD. Drugs and oral disorders. *Periodontol* 2000. 1998;18:21–36.
- [29]. Epstein JB, Gorsky M, Guglietta A, Le N, Sonis ST. The correlation between epidermal growth factor levels in saliva and the severity of oral mucositis during oropharyngeal radiation therapy. *Cancer*. 2000;89:2258-65.