

# Innovations

## Knowledge, attitude and perception on salivary diagnostic markers among oral medicine specialist

**Dr. Divyadarshini V**

PG Student

Department Of Oral Medicine and Radiology

Saveetha Dental College and Hospitals

SIMATS

Chennai, Tamil Nadu, India.

**Dr. T.N. Uma Maheswari**

Professor and Head of the Admin

Department of Oral Medicine and Radiology

Saveetha Dental College and Hospitals

SIMATS

Chennai, Tamil Nadu, India.

Corresponding Author & Email: **Dr. T.N. Uma Maheswari**, [umamaheswaritn@saveetha.com](mailto:umamaheswaritn@saveetha.com)

Received: 17 May 2022 Accepted: 20 June 2022 Published: 30 June 2022

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### **Abstract:**

**Aim:** This study was conducted to assess the knowledge, attitude and perception of salivary diagnostic markers among Oral Medicine Specialists. **Background:** Early diagnosis plays a crucial role in planning the management strategy and improving the prognosis of disease. Saliva serves as a potential diagnostic fluid as it is economic, non-invasive and gives information about oral & general health. Saliva can be used for clinical diagnosis, disease monitoring and decision making. Salivary constituent's serve as effective indicators of local and systemic disorders. **Materials and methods:** A 12 multiple choice questionnaire was prepared and circulated among peers for validation. An online survey was created using google forms and distributed among Oral Medicine Specialists. Data was tabulated in Excel spreadsheets, imported to IBM SPSS software version 2.0 and statistical analysis were performed. Frequency, percentage and chi square test were performed. **Results:** Oral medicine specialists were mostly aware about recent salivary diagnostic markers. Majority of the participants believe that salivary biomarkers can serve as a diagnostic & prognostic tool. 70% of the participants feel that saliva can replace tissue or serum as a biomarker and can be translated into routine clinical practice. **Conclusion:** Oral medicine specialists have adequate awareness and knowledge about salivary diagnostic markers, but certain knowledge has to be brushed up among them. Majority of participants showed a positive attitude towards using salivary markers as a diagnostic & prognostic tool. Furthermore, it is important to train dental students on these grounds to help them treat their patients in the best possible way.

**Keywords:** 1.Attitude, 2.Diagnostic markers, 3.Knowledge, 4.Oral Potentially Malignant Disorders, 5.Precancerous conditions, 6.Salivary markers.

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## Introduction

Saliva is mainly produced by three major salivary glands namely the parotid, submandibular, and sublingual glands. Numerous minor salivary glands are distributed throughout the mouth extending into the tracheobronchial tree, they also aid in salivary production. Saliva is a clear, slightly acidic (pH 6.0–7.0) heterogeneous fluid that is composed of 98% water and 2% other compounds such as electrolytes, mucus, antibacterial compounds, and various enzymes.<sup>[1]</sup> Saliva consists of secretions from salivary gland, gingival crevicular fluid, expectorated bronchial and nasal secretions, serum and blood derivatives from oral wounds, bacteria and their products, viruses, fungi, desquamated epithelial cells, other cellular components, as well as food debris.<sup>[2]</sup> Saliva can be used for clinical diagnosis, disease monitoring and decision making. Salivary constituent's serves as an effective indicator of local and systemic disorders.

The practice of using saliva as an indicator for detecting the state of human body dates back centuries. Cytochemical procedures using saliva samples to identify biomarkers and to better understand disease has been employed in gout and rheumatism.<sup>[3]</sup> Early attempts to use saliva for diagnostic purposes was based on the notion that specific biomarkers already known to be present in serum must also be present in saliva. Granted that this presumption appeared, and is now known, to be largely accurate, accounting for how biomarkers made their way into saliva remained confounding. Furthermore, limitations posed by the available technical methods of saliva collections, coupled with a lack of standardized parameters for collection and storage, sometimes translated into considerable difficulty with detection of low-level markers at that time.

Comparatively, saliva carries many advantages over blood. Collection is easy and undemanding. While blood sampling requires highly trained personnel, saliva procurement can be done by anyone, including self-collection.<sup>[4]</sup> Sample collection procedure is non-invasive. Sample procurement is painless, reducing the discomfort most individuals endure from biopsies and repeated blood draws, while encouraging others to participate in timely medical evaluations and screenings. Samples are safer to handle. Salivary secretions contain factors that inhibit the infectivity of HIV, resulting in extremely low or negligible rates of oral transmission. Samples are easier to ship and store. Saliva does not clot and requires less manipulation than blood. The procedure is economical. Saliva is easily collected, shipped, and stored, resulting in decreased overall costs for patients and health care providers.<sup>[5]</sup>

Unstimulated whole saliva, also called resting saliva, is composed mainly of submandibular gland saliva together with saliva from sublingual gland and minor salivary glands.<sup>[6]</sup> The characteristics of unstimulated saliva are that it is more viscous and is mucin-rich. Stimulated whole saliva is mainly composed of parotid gland saliva and to some extent saliva from the submandibular gland that is produced upon stimulation. Characteristics of stimulated saliva reveal that it is thin, watery and amylase-rich.

Several types of inflammatory biomarkers associated with oral diseases and systemic diseases have been detected in saliva such as interleukins-1b, -6 and -8 (IL-1b, -6 and -8), tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) and matrix metalloproteinases (MMP)-8 and -9. Various diseases, such as heart diseases, oral malignancy, breast cancer, and acquired immunodeficiency syndrome are being identified by increasing expression of specific molecular markers.<sup>[7]</sup>

Sialo chemistry offers great value in the diagnosis of Sjogren's Syndrome. An increase in the levels of immunoglobulins, inflammatory mediators, albumin, sodium, and chloride and a decrease in the level of phosphate are indicative of Sjogren's Syndrome. Elevated level of, lactoferrin beta 2 microglobulin, lysozyme C, and cystatin C were seen in salivary protein analysis. However, the levels of salivary amylase and carbonic anhydrase were decreased.<sup>[8]</sup>

Oral cancer ranks as the 11<sup>th</sup> most prevalent cancer worldwide, and among all oral malignancies, oral squamous cell carcinoma (OSCC) is the most predominant, constituting about 90% of all oral cancers.<sup>[9-13]</sup> Despite great progress in chemo/radiotherapy, and targeted therapy, the prognosis of OSCC is poor and aggressive local invasion and metastasis causes recurrence.<sup>[14]</sup> Radiation therapy and chemotherapy used in management of oral cancer can result in stomatodynia, dysphagia, changes in taste perception and xerostomia. Secondary bacterial, viral and fungal infections form another spectrum of the mucositis

associated illness.<sup>[15]</sup>Early detection plays a crucial role in treatment planning and prognosis.<sup>[16,17]</sup> The upregulation of salivary miRNA 184, and miRNA 21 and downregulation of salivary miRNA 145 can be used as potential biomarkers to predict malignant transformation. Of these three, salivary miRNA 184 had the highest sensitivity and specificity.<sup>[18]</sup>Previous studies have concluded that salivary miRNA-21 can be utilized as a potential adjuvant diagnostic biomarker to evaluate very early malignant changes in OPMD; its potential was much higher when compared to salivary miRNA-31.<sup>[19-22]</sup>The aim of this survey was to assess the knowledge, attitude and perception of salivary diagnostic markers among Oral medicine specialists.

**Materials and methods**

This is a cross-sectional study based on self-reported questionnaires. A questionnaire with 12 items was framed and developed using google forms, with a consent form appended to it. Link of the questionnaire was sent through emails, WhatsApp and other social media. Participants with access to the internet was able to participate in the study. Participants with age more than 18 yrs., able to understand English language, who are pursuing or completed their master degree in Oral Medicine and willing to give informed consent were included. Ethical approval for conducting the survey was obtained from the Institutional Human Ethics Committee. All the data were collected and compiled by the author. Simple random sampling method was used to enrol the participants for the study. This provides a chance for equal odds of every member of the population to be chosen as a participant in the study. The primary items of the questionnaire were reviewed by peers who provided feedback and suggested necessary changes in order to establish validity of the survey questionnaire.

Online self-reported questionnaires developed, which contained 15 multiple choice questions. Afterwards, the reliability of the questionnaire was established using a pilot test by collecting data from 20 dentists not included in the study sample. They were asked to fill in the questionnaire individually and were encouraged to think loudly and to speak what they meant by each answer and how they understood each question. Excel spreadsheets were used for data collection and manipulation. Age, gender, profession, knowledge, attitude and perception were assessed. Output collected as nominal values, so percentage was calculated and the results were tabulated. Results were represented by pie charts and bar graphs. Data were statistically analysed using IBM SPSS software version 20. Data were described using frequencies and percentages. Chi-square was used to analyse differences between categorical variables. A p-value of less than 0.05 was considered statistically significant.

**Results**

Study was conducted among 150 Oral Medicine specialists, out of which 55 were males (37%) and 95 (63%) were female, which is given in Table 1.

**Table 1: Gender distribution**

Gender	Frequency	Percentage
Males	55	37%
Females	95	63%

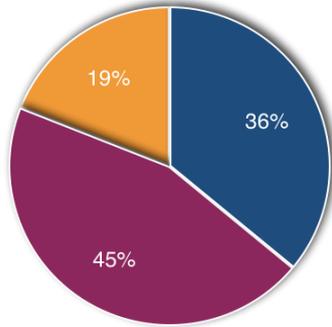
**Table 1 showing frequency and percentage distribution of gender**

36% were first year MDS students, 45% were second year MDS students and 19% were third year MDS students, given in Graph 1. 50% were senior lecturer, 25% were readers, 15% were associate professors and 10% were professors, given in Graph 2. Among the oral medicine specialists, 62% had less than 5

years of practice, 19% had 5-10 years of practice, 17% had 10-15 years of practice and 2% had more than 15 years of clinical practice; given in Graph 3.

**Graph 1: Year of study of PG students**

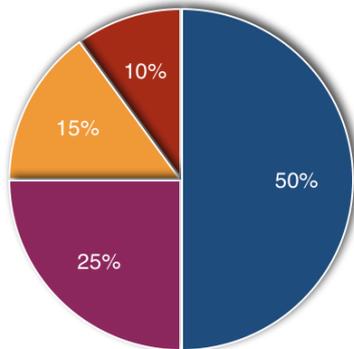
● I MDS    ● II MDS    ● III MDS



**YEAR OF STUDY - PG STUDENTS**

**Graph 2: Designation of faculty member**

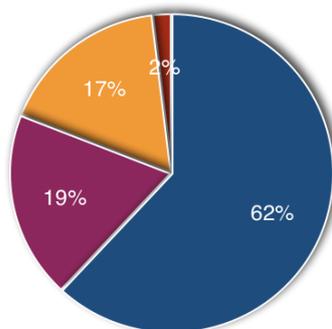
● SENIOR LECTURER    ● READER  
● ASSOCIATE PROFESSOR    ● PROFESSOR



**DESIGNATION OF FACULTY MEMBER**

**Graph 3: Years of practice of Practitioners**

● LESS THAN 5 YRS    ● 5-10 YRS  
● 10-15 YRS    ● MORE THAN 15 YRS

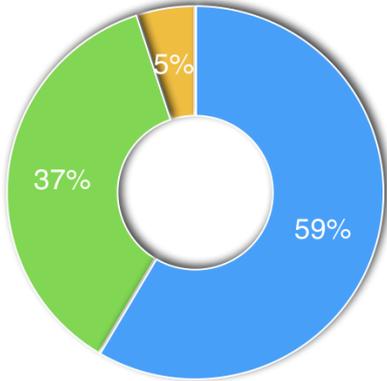


**YEARS OF PRACTICE**

Graph 4 shows participants' knowledge on salivary protein increases in Sjogren's Syndrome. 89 (59%) participants answered lactoferrin, beta 2 microglobulin, lysozyme C and cystatin C increased in Sjogrens syndrome. 56 (37%) participants answered salivary amylase and carbonic anhydrase increased in Sjogrens syndrome. 8 (5%) participants answered that beta 2 microglobulin and salivary amylase were increased in Sjogren's syndrome.

**Graph 4: Salivary protein increased in Sjogrens syndrome**

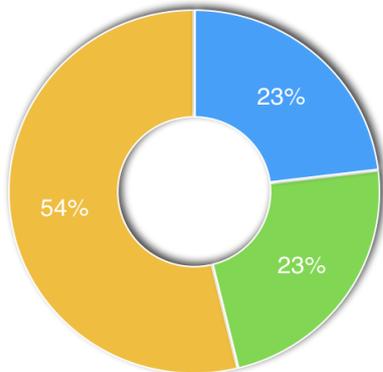
- Lactoferrin, beta 2 microglobulin, lysozyme C, cystatin C
- Salivary amylase, carbonic anhydrase
- Beta 2 microglobulin, salivary amylase



Graph 5 shows participants' knowledge on genomic salivary markers in detecting early malignancy. 81 (54%) participants answered miRNA 184, miRNA 21 and miRNA 145. 35 (23%) participants answered miRNA 120 and miRNA 157. 35 (23%) participants answered miRNA 31 and miRNA 65.

**Graph 5: Genomic salivary markers in detecting early malignancy**

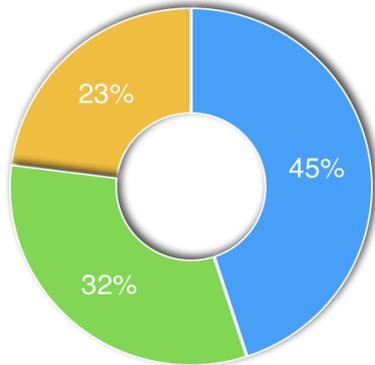
- miRNA 120, miRNA 157
- miRNA 31, miRNA 65
- miRNA 184, miRNA 21, miRNA 145



Graph 6 shows participants' knowledge on proteomic salivary markers in detecting early malignancy. 68 (45%) participants answered IL-8, IL-1 and TNF- $\alpha$ . 48 (32%) participants answered TGF- $\beta$  and lysozyme. 35 (23%) participants answered C-reactive protein and salivary alpha amylase.

**Graph 6: Proteomic salivary markers in detecting early malignancy**

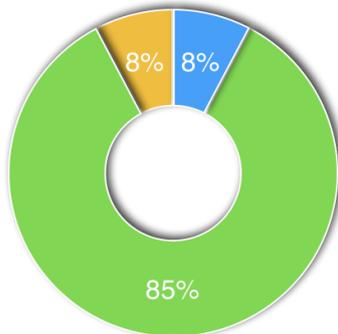
- IL-8, IL-1, TNF - alpha
- TGF-Beta, Lysozyme
- C-reactive protein, salivary alpha amylase



85% participants preferred the spit method, 8% preferred drool and 8% preferred oral rinse method for saliva collection, given in graph 7. 50% responded that saliva needs to be transported within 12-24 hours, 43% responded to transportation within 24-48 hours and 7% responded to transportation within 36-72 hours, given in graph 8.

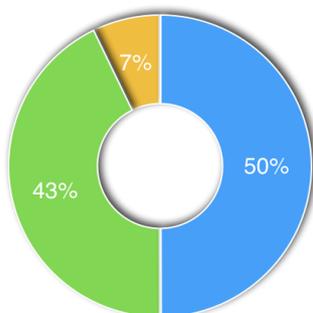
**Graph 7: Saliva Collection Method**

- Drool
- Spit
- Oral Rinse



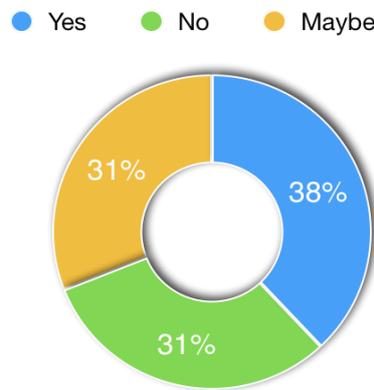
**Graph 8: Salivary Sample Transportation**

- 12-24 hrs
- 24-48 hrs
- 36-72 hrs

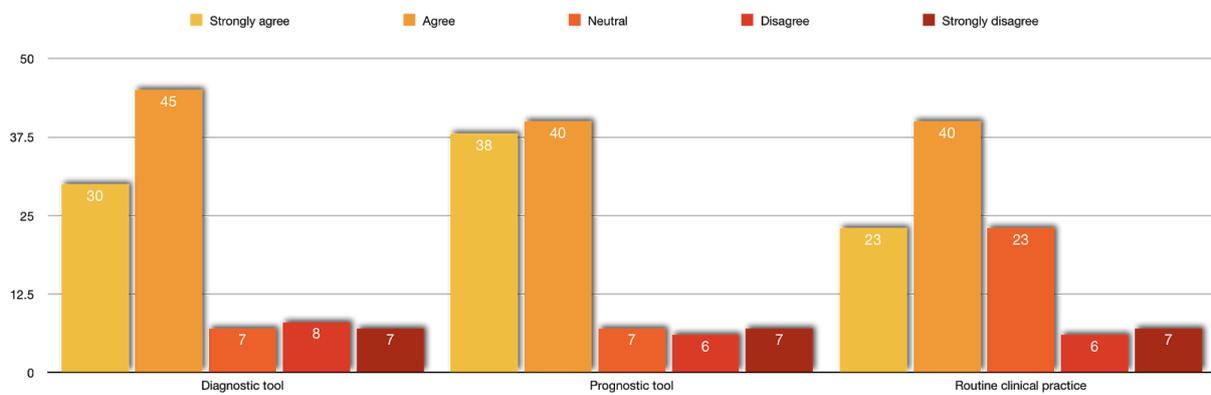


38% participants believed that saliva can replace tissue and serum for detection of Oral Potentially Malignant Disorders. 31% were doubtful and 31% replied negatively (Graph 9). Graph 10 represents the participants attitude towards salivary biomarkers as a diagnostic tool, prognostic tool and whether it can be employed in routine clinical practice.

**Graph 9: Can saliva replace tissue & serum for detection of OPMD**



**Graph 10: Salivary biomarkers for OPMD & OSCC**



### Discussion

This study was conducted among 150 Oral Medicine specialists, out of which 55 were males (37%) and 95 (63%) were females. Most of the participants were senior lecturers and had less than 5 years of experience. Most of the participants had sufficient knowledge about salivary protein increase in sjogren's syndrome, genomic salivary marker and proteomic salivary markers in detecting early malignancy. Literature search revealed no other studies conducted on knowledge, awareness and perception of salivary markers in sjogrens syndrome or early detection of malignancy. A Survey conducted among the general dentist revealed that awareness among dental students about salivary markers in caries detection is fair and there is the need for continuous education and for formal inclusion of the methods used in detection of caries, in the students' curriculum.<sup>[23-26]</sup> The results of Zahran et al. study revealed upregulated miRNA 184 with an area under the curve (AUC) of 0.86 and miRNA 21 with an AUC of 0.73 and downregulated miRNA 145 with an AUC of 0.68, which proved that these miRNAs are significant in detecting early malignancy in OPMD and should be further analyzed in various populations.<sup>[27-30]</sup> Majority of the participants believed that salivary biomarkers can serve as a diagnostic and prognostic tool. Most of them had a positive attitude that it can be translated into routine clinical practice. Early detection of disease plays a crucial role for treatment planning and prognosis. Saliva has great potential as a diagnostic fluid and offers advantage over serum and other biological fluids by an economic and non-invasive collection method for monitoring of systemic health and disease progression. The plethora of components in this fluid can act as biomarkers for diagnosis of various systemic and local diseases.<sup>[31-33]</sup>

Since it was an online study, not many people from older age groups participated in the survey and the study was limited to the participants with access to the internet, who had smartphones and e-mail IDs. And the survey was in English so people who understand English could only participate.

### Conclusion

To conclude, this study provides evidence regarding knowledge, awareness and perception on salivary diagnostic markers. Oral medicine specialists have adequate awareness and knowledge about salivary diagnostic markers, but certain knowledge has to be brushed up among them. Majority of participants showed a positive attitude towards its use as a diagnostic & prognostic tool. Furthermore, they need to be trained on these grounds to help them treat their patients in the best possible way.

### Financial support and sponsorship

Study funded by Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, Tamil Nadu.

### Conflict of interest

There are no conflicts of interest.

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