

## UTILITY OF SALIVARY CA-125 AND LDH AS A TUMOR MARKER IN ORAL MALIGNANCY

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### ABSTRACT

**Background:** The mortality and morbidity associated with oral Squamous cell carcinoma (OSCC) can be greatly reduced if tumor markers which can detect OSCC at an early stage are available. This study attempts to use saliva as the diagnostic medium to determine the correlation of salivary CA 125 and LDH in tobacco users with and without potentially malignant disorders. Changes in CA 125 and LDH level can be used as a marker in patients with and without premalignant disease and can be used as a deterrent in continuation of the habit. **Aims:** To assess the role of CA 125 & LDH as a tumour marker in Oral cancer patients. **Materials and methods:** Cross sectional observational study. Time period: December 2015 to August 2017. Study area: OPD of tertiary care hospital in pune. Total participants: 150 persons. Under non-stimulatory conditions whole saliva sample was collected from each individual and was centrifuged. The resulting supernatant was used for estimation of CA 125 and LDH levels. **Results:** In present study, mean Salivary LDH level was found to be lowest among cases of healthy individuals while it was highest among individuals who were diagnosed and underwent treatment for malignancy. However there was insignificant difference seen between levels of diagnosed case of oral malignancy and the ones who underwent treatment for oral malignancy. Also mean Salivary CA-125 was lowest in healthy individuals and highest in individuals diagnosed with oral malignancy and the levels were seen to be reduced significantly in the one who underwent treatment for oral malignancies than those who didn't. **Conclusion:** Salivary CA 125 and LDH has a role in early detection of oral malignancies and can be used as a diagnostic marker. However LDH levels are persistently raised even after treatment for oral malignancy.

**KEYWORDS:** Oral squamous cell carcinoma; Tumour markers; Salivary CA125; LDH.

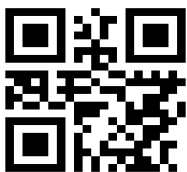
### INTRODUCTION

Oral cancer refers to all malignancies arising from the lips, alveolus, floor of mouth, cheek, tongue, gingiva and pharynx [1]. It is one of the major global public health problems and is the sixth most common human malignancy with a five year mortality rate of almost 50% [2]. This has not changed significantly over the last 50 years [3]. It is the commonest cancer in males and the third commonest cancer in females in India. More than 90% of tumours of the oral cavity are squamous cell carcinoma arising from the oral mucosa [4]. Squamous cell carcinoma occurs mostly in men aged 45 years and older and is associated with tobacco and alcohol consumption [5]. A high prevalence of oral cancer

in India and other Asian countries has been attributed to the influence of region specific epidemiological factors such as tobacco and betel quid chewing [6]. Oral cancer is a major problem in the Indian subcontinent where it ranks among the top three types of cancer in the country [7].

Age-adjusted rates of oral cancer in India is high i.e. 20 per 100,000 population and accounts for over 30% of all cancers in the country [8]. Another alarming scenario is the increasing incidence of oral squamous cell carcinoma (OSCC) in younger people owing to the heavy abuse of alcohol, tobacco and tobacco related products. Even though clinical diagnosis occurs via examination of the oral cavity and tongue which is easily accessible by current diagnostic tools, the majority of cases present to a healthcare facility at later stages of cancer, thereby reducing chances of survival due to delay in diagnosis [9].

Tumour markers are substances present in, or produced by, a tumour itself or produced by a host in response to a tumour that can be used to differentiate a tumour from normal tissue or to determine the pres-



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ence of a tumour based on measurements in blood or secretions [10, 11]. Tumour markers include various substances like cell surface antigens, cytoplasmic proteins, enzymes, hormones, oncofetal antigens, receptors, oncogenes and their products [10]. These substances can be found in blood, saliva, urine, stool, tumour tissue, or other tissues or bodily fluids of patients with cancer.

Tumour markers are very useful in monitoring the course of a diagnosed malignant tumour, for example their levels decrease in response to treatment and increase when the cancer recurs or is irresponsive to any treatment modality. When used in combination with other investigations the changed levels of tumour markers can be extremely useful in the detection and diagnosis of cancer [12]. Currently biopsy is considered to be a gold standard diagnostic technique for diagnosing oral malignancy.

The purpose of this study was to assess that salivary CA-125 and LDH can be used as a potential tumour markers for early diagnosis and treatment of OSCC.

**Aim:-**To assess the role of CA 125 & LDH as a tumour marker in Oral cancer patients.

**Objectives:-** 1) To estimate the levels of salivary CA 125 and LDH in following groups

#### MATERIALS AND METHODS

**Study design:** cross sectional observational study.

**Ethics approval:** This study was approved by the ethical committee of our institute

**Study Period:** December 2015 to August 2017.

**Study location:** Bharati Hospital, Pune. (Tertiary care centre)

**Study population:** 90 random patient presenting with oral pathology, 30 individuals addicted to tobacco.

And 30 individuals who are in good health without any addiction.

**Inclusion criteria:** All patients above 18 years, attending Bharati hospital surgery OPD for Oral pathology were included in this study

**Exclusion criteria:** Patients with a history of any other malignancy. Subjects with psychiatric disorders who can't give consent.

**Grouping:** Group 1: 30 absolutely healthy individuals with no habit of tobacco chewing, smoking and alcohol.

Group 2: 30 healthy tobacco users and smokers without apparent clinical oral lesion.

Group 3: 30 patients with proven Pre malignant lesions in oral cavity.

Group 4: 30 diagnosed case of oral cancers for the first time.

Group 5: 30 patients who have undergone surgery and coming for regular follow up and are in 3rd month after surgery.

#### Methodology

Under non-stimulatory conditions 5cc whole saliva sample was collected from each individual of all the groups in a wide mouth container. Saliva sample was immediately centrifuged at 3000 rpm for 10 minutes to remove squamous cells and debris. The resulting supernatant fluid was subjected to ELISA for assessment of CA 125 and LDH levels. [13]

**Statistical analysis:** The collected data was coded and entered in Microsoft Excel sheet. Mean, SD and Median was calculated for quantitative data. Salivary concentrations of CA125 in normal, premalignant lesion and oral squamous cell carcinoma patients were compared using Mann-Whitney U test.

#### RESULTS

The study covered total of 150 subjects divided into 5 groups. Salivary sample was collected from each of these individuals to assess the level of CA -125 and LDH. Advantages of salivary sample collection were that it was noninvasive, easy, safe and inexpensive. The sample collection did not require any trained medical staff. It could be collected anywhere. Also, it was easy to store and transport to the laboratory.

Of these 71 % were males and 29% were females. Overall higher male prevalence was seen among cases with pre- malignant and malignant oral cavity lesions.

The mean age of the cases with pre-malignant and malignant oral cavity lesions was 51.73 years and 55.87 years respectively.

Also mean Salivary CA-125 was lowest in group 1 and highest in group 4 and the levels were seen to be reduced significantly in group 5 as compared to group 4. (Table 1)

In present study, mean Salivary LDH level was found to be lowest among cases of group1 while it was highest among cases of group 5. However there was insignificant difference seen between levels of group 4 and group 5. (Table 2)

**Table 1. Comparison of mean salivary CA-125 levels among study groups.**

Variables	Group	Mean±SD	p- value
Salivary-CA-125 (mg/dl)	1	33.00±24.37	Total p – value in all the groups was <0.01 (Group1 vs group 2,3,4 5 Group 2 vs group3,4,5 Group 3 vs group 4,5 Group 4 vs group 5 )
	2	296.67±161.4	
	3	809.64±561.7	
	4	1362.19±523.3	
	5	888.15±306.1	

**Table 2. Comparison of mean salivary LDH levels among study groups.**

Variables	Group	Mean	p- value
Salivary LDH (mg/dl)	1	63.04±47.4	Total p value in all the groups was <0.01 (Group 1 vs group 3, 4, 5 Group 2 vs group 3, 4, 5 Group 3 vs group 4, 5)
	2	231.67±196.44	
	3	786.23±432.67	
	4	1515.17±765.14	
	5	1518.13±1315.99	

## DISCUSSION

Oral cancer, when found early, has an 80 to 90% survival rate. Despite this fact and great treatment advances, the World Health Organization has reported oral cancer as having one of the highest mortality ratios amongst other malignancies with a death rate at five years from diagnosis (45%) [14]. This high morbidity rate can definitely be attributed to the late diagnosis of the disease [15].

Tumour markers are very useful in monitoring the course of a diagnosed malignant tumour, for example pre-treatment and subsequent serial values are essential for the evaluation of the response to the treatment modality with time. When used in combination with biopsies and other tests the detection of tumour markers in the blood can be extremely useful in the early detection of cancer thereby significantly improving its prognosis[12].

The present study was thus conducted to assess the role of Salivary CA 125 & LDH as a tumour marker in Oral Cavity cancer. The study included total of 150 subjects, 30 each groups as mentioned earlier in Table 1. and 2.

LDH represents a marker to cell death and tissue breakdown and its raised level often signifies a disease process [16]. CA125 is a repeating peptide epitope of the mucin MUC16 [17,18], which promotes cancer cell proliferation and inhibits anti-cancer immune responses [19-22]. CA125 has been extensively investigated as a biomarker in three separate clinical scenarios as a screening test for the early detection of cancer, to distinguish between benign and malignant disease and to monitor response to therapy.

In present study, overall higher male prevalence was seen among cases with pre-malignant (group3) and malignant (group4) oral cavity lesions whereas there are studies having the highest incidence of oral cancer in the world with significant male preponderance[23] just like ours.

The mean age of the cases with pre-malignant (group3) and malignant (group4) oral cavity lesions in this study was 51.73 years and 55.87 years respectively. Aggarwal R et al.[24] in their study of total 133 cases found mean of 50.16 years. Similar results were also reported by Pudasaini S et al. [25]with mean age of 51.6 years. Similar results were also observed by other authors [26,27].

In our study, mean Salivary LDH level was lowest among controls(group1) (63.04 mg/dl) while it is highest among cases of oral carcinoma after treatment (group5)(1518mg/dl )also there was insignificant difference among cases of carcinoma before (group4)(1515 mg/dl) and after treatment (group5)(1518.13 mg/dl). LDH Levels were able to differentiate between cases with pre malignant lesions (group3) (786.23 mg/dl) and healthy controls (group1) (63.04 mg/dl). Also, significant difference was noted between healthy controls (group1) (63.04 mg/dl) and healthy tobacco users (group2) (231.67 mg/dl). A similar study was conducted by Shpitzer et al.[28] and it was found that salivary LDH was significantly higher in the patients with OSCC compared to the control group (p<0.05). Nagler et al.[29] in their study observed raised level in both pre-malignant and malignant oral mucosa pathologies. Joshi et al.[30] in their study observed the mean lactate level in control, pre-malignant and OSCC group as 267.2 IU/L, 519.36 IU/L and 788.73 IU/ L respectively (p<0.01). Shpitzer et al.[28] and Shpitzer et al.[31] also found total salivary LDH levels to be high in oral cancer patients. Our results are also comparable with the study done by Shetty et al.[32] who have reported consistently higher salivary LDH levels in oral precancer and cancer patients as compared to healthy controls.

In this study, mean Salivary CA-125 level was very well able to distinguish between control (group1), premalignant (group3) and malignant lesions (group4) with lowest values seen among controls (group1) (33.0 mg/dl) followed by healthy tobacco users (group2) (296.67 mg/dl), cases with pre malignant lesions (group3) (809.64 mg/dl) and it was highest among cases of oral carcinoma (group4) (1362.2 mg/dl). Also the levels salivary CA-125 were seen to be reduced significantly post-operatively in patients of group 5 (888.15 mg/dl) as compared to patients with oral malignancy in group 4 (1362.2 mg/dl) Balan et al.[13] in a similar study observed the mean salivary CA 125 values of OSCC patients as 320.25 and that of control group as 33.14 (p<0.05). Rihan M et al. [33], observed the level of salivary CA-125 as 342.65 U/ml in cases of OSCC which was significantly increased compared with 203.65 U/ml in the healthy controls, (P 0.017). The authors concluded that salivary CA-125 can be a potential tumor marker for OSCC. Geng XF et al. [34] in their study also observed significant difference in CA-125 levels among patients with OSCC than in patients with non-neoplastic disease and healthy controls, however contrary to our findings CA-125 levels were not significantly different

between patients with non-neoplastic disease and controls.

## CONCLUSION

These observations showed that salivary CA 125 and LDH has a role in early detection of oral malignancies and differentiating between premalignant and malignant lesions. The present study was done in a limited population, thus needs further evaluation in larger cohort studies to see the role of high CA-125 and LDH level among tobacco chewers and its prognostic value in cases who quit or continued tobacco chewing and developed OSCC.

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