

ORIGINAL ARTICLE

A prospective study for Assessment of saliva CA- 125 level in oral cancer patients

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ABSTRACT

Aim: To detect CA- 125 level in saliva of oral cancer patients.

Methodology: A total of fifty- six SCC patients and thirty healthy subjects were selected. A non- stimulated whole saliva (5cc) was collected and evaluated for CA- 125 level ELISA.

Results: A higher salivary CA 125 level (514.2 ± 132.6 U/mL) was observed in poorly differentiated SCC followed by moderately differentiated (340.6 ± 80.2 U/mL) and minimum values was observed in well differentiated SCC (236.2 ± 76.2 U/mL). The mean \pm SD CA- 125 level in group I patients was 428.5 ± 110.2 U/mL and in group II was 132.4 ± 58.6 U/mL. Higher salivary CA 125 level (520.5 ± 168.4 U/mL) was observed in stage IV and minimum in stage I (165.2 ± 46.2 U/mL) which was statistically significant ($P < 0.05$).

Conclusion: Patients with poorly differentiated SCC, cases of buccal mucosa and stage IV exhibited higher values of salivary CA- 125 level as compared to healthy control.

Key words: Oral Cancer, Saliva, Tongue, CA- 125

INTRODUCTION

Oral cancer is major reason of death. It is the second highly prevalent head and neck cancer having high deaths and morbidity in males and third in females after lung cancer. Oral cancer patients have 5 years mortality of 50%.¹ Among all cancer of mouth, oral squamous cell carcinoma (OSCC) is the most common one. Dorsum and lateral border of tongue, mouth floor, lips, buccal mucosa, alveolus, pharynx and gingiva are potential site of its occurrence.² Depending upon the geographical area, it has specific site of origin. Asian population has high tendency of involvement of buccal mucosa while Europeans and American show tongue as commonest site. Tobacco and alcohol are causative agent for SCC.³

The high prevalence of SCC in Indian and Pakistan is due to increased rate of alcohol consumption and tobacco usage in various forms such as chewing and non- chewing tobacco. Gutkha, Pansupari, Zarda, betel quid, mawa, mishri are various non- smoking forms of tobacco whereas bidi, cigarette, hukli, hookah, cigar are smoking forms of tobacco.⁴ The occurrence of SCC depends on intensity and frequency of tobacco products usage. The peak age range is above 45 years. However, in the last couple of years young individuals also show increase incidence owing to high tobacco consumption in this age group.⁵

Tumour markers are produced by either tumour or host against tumour in the secretions. There are various forms of tumour markers such as enzymes, proteins and hormones etc. Common secretion where these markers are found are saliva, blood, urine and other tissues. Thus, saliva may be regarded as a diagnostic aid to detect tumour markers for SCC because it is safe, simple, non-

expensive, painless and non- invasive method.⁶ Cancer antigen (CA- 125) is widely used tumour marker in SCC. 5 to 80 U/ml is normal value for CA- 125. Outer surface of cancer cells sheds CA 125 into saliva and blood. SCC patients exhibit higher CA- 125 level.⁷ Considering this, we attempted present study with the aim to detect CA- 125 level in saliva of SCC patients.

METHODOLOGY

This cross- sectional observation study was conducted following approval from review and ethical committee with written informed consent from all patients as well as healthy subjects. Patient consent followed declaration of Helsinki. The study duration was of 8 months. Patients above 18 years irrespective of sex with written consent were selected. Patients with psychiatric disorder, pregnant women etc. were excluded.

Fifty- six SCC patients and thirty healthy subjects were selected. Grouping was done as group I comprised of SCC patients and group II as control (healthy). Histological grading as well differentiated, moderately differentiated and poorly differentiated was performed. Staging of OSCC was also done.

Estimation of CA- 125: A non- stimulated whole saliva (5cc) was collected in wide mouth container from all subjects. It was subjected to centrifugation for 10 minutes at 3000 rpm. Resultant supernatant fluid was separated and evaluated for CA- 125 level using enzyme-linked immunosorbent assay (ELISA) using the CA125 quantitative assay kit.

Statistical analysis: All findings of the study were represented as mean, numerical and percentages. SPSS

version 20.0 was used for the study. One way ANOVA test compared CA- 125 values between various groups and subgroups. The level of significance <0.05 was considered significant.

RESULTS

Table 1 Clinical characteristics

Variables	Number	Percentage
Age group		
20-30	7	12.5
30-40	25	44.6
40-50	14	25
50-60	10	17.8
Site		
Labial mucosa	3	5.3
Buccal mucosa	32	57.1
Tongue	15	26.7
Palate	2	3.6
Alveolar ridge	3	5.3
Lips	1	1.8
Gender		
Male	42	75
Female	14	25
Grading		
Well differentiated	10	17.8
Moderately differentiated	26	46.4
Poorly differentiated	20	35.7
Stage		
I	8	14.2
II	11	19.4
III	20	35.7
IV	17	30.3

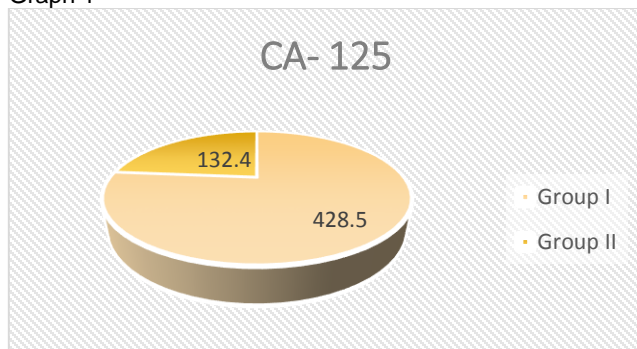
Maximum cases were presented in age group 30-40 years ie 25 (44.6%) followed by 40-50 years 14 (25%), 50-60 years 10 (17.8%) and 20-30 years 7(12.5%). Common site was buccal mucosa 32 (57.1%), tongue 15 (26.7%), labial mucosa 3 (5.3%), alveolar ridge 3 (5.3%), palate 2 (3.6%) and lips 1 (1.8%). There were 42 (75%) males and 14 (25%) females. Grading was well differentiated in 10 (17.8%), moderately differentiated in 26 (46.4%) and poorly differentiated in 20 (35.7%) cases. Stage was I in 8 (14.2%), II in 11 (19.4%), III in 20 (35.7%) and IV in 17(30.3%) (Table 1).

Table 2 Salivary CA 125 levels

Groups	CA 125 (Mean± SD)	P value
Group I	428.5± 110.2	Significant <0.05
Group II	132.4± 58.6	

ANOVA, Significance <0.05

Graph 1



The mean± SD CA- 125 level in group I patients was 428.5± 110.2 U/mL and in group II was 132.4± 58.6 U/mL which was statistically significant (P< 0.05) (Table 2, Graph 1).

Table 3 Salivary CA 125 levels based on staging

Stage	Mean± SD	P value
I	165.2±46.2	Significant <0.05
II	270.4±84.2	
III	384.2±112.4	
IV	520.5±168.4	

ANOVA, Significance <0.05

Higher salivary CA 125 level (520.5±168.4 U/mL) was observed in stage IV and minimum in stage I (165.2±46.2 U/mL) which was statistically significant (P< 0.05) (Table 3, Graph 2).

Graph 2

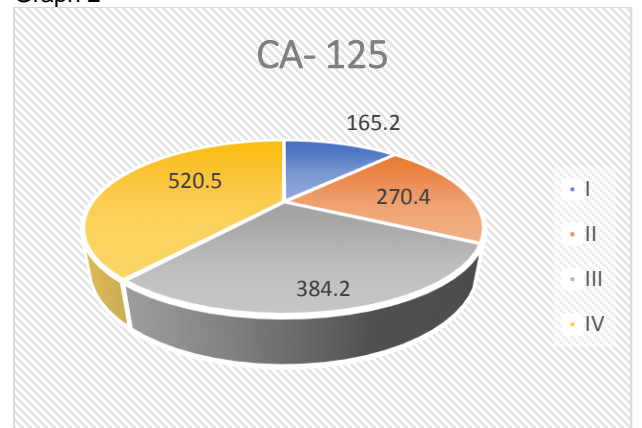
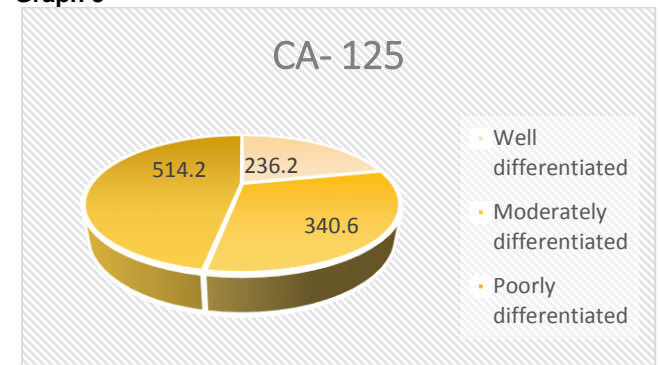


Table 4 Salivary CA 125 levels based on Histopathological grading

Stage	Mean± SD	P value
Well differentiated	236.2±76.2	Significant <0.05
Moderately differentiated	340.6±80.2	
Poorly differentiated	514.2±132.6	

ANOVA, Significance <0.05

Graph 3



Higher salivary CA 125 level (514.2±132.6 U/mL) was observed in poorly differentiated SCC followed by moderately differentiated (340.6±80.2 U/mL) and minimum

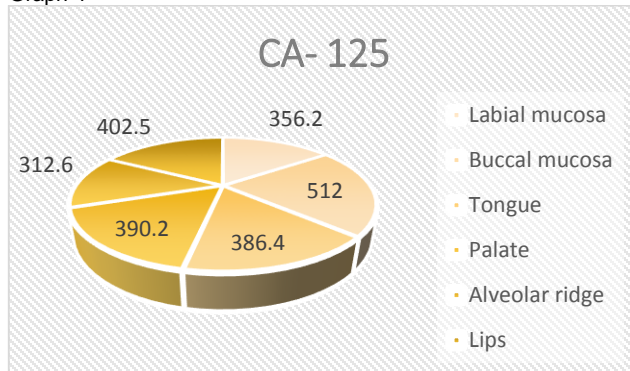
values was observed in well differentiated SCC (236.2±76.2 U/mL) which was statistically significant ($P < 0.05$) (Table 4, Graph 3).

Table 5 Salivary CA125 levels based on different sites

Site	Mean± SD	P value
Labial mucosa	356.2±113.6	Significant <0.05
Buccal mucosa	512.0±124.2	
Tongue	386.4±130.5	
Palate	390.2±132.8	
Alveolar ridge	312.6±165.7	
Lips	402.5±236.2	

The mean salivary CA- 125 level in SCC patients of labial mucosa was 356.2±113.6 U/mL, buccal mucosa was 512.0±124.2 U/mL, tongue was 386.4±130.5 U/mL, palate was 390.2±132.8 U/mL, alveolar ridge was 312.6±165.7 U/mL and lips was 402.5±236.2 U/mL which was statistically significant ($P < 0.05$) (Table 5, Graph 4).

Graph 4



DISCUSSION

Oral squamous cell carcinoma is the highly prevalent cancer among men especially those who consume tobacco products. Depending upon the type of tobacco product, the location of OSCC is decided.⁸ Patients consuming chewable tobacco are more prone to SCC of labial mucosa, buccal mucosa and mouth floor and those use smoking form of tobacco (bidi, cigarette) are liable for involvement of palate. Initially potentially malignant disorders like lichen planus, oral submucous fibrosis (OSMF) and leukoplakia appears in the oral cavity. All of them have high malignant potential. Stomatitis nicotina palatinus also known as smokers' palate is associated with bidi and cigarette smoking.⁹ Tobacco pouch keratosis is lesion seen in vestibules such as labial and buccal vestibules. The role of alcohol is to make the oral mucosa dry and permeable to oral carcinogens such as aromatic hydrocarbons, tar and nicotine etc. Once permeability to these agents increases, the penetration of products to deeper tissues is enhanced leading to oral cancer.¹⁰

Our single centre, randomized study enrolled 56 histological confirmed cases of OSCC and thirty healthy subjects. It was seen that CA- 125 level in SCC patients was 428.5± 110.2 U/mL and in controls was 132.4± 58.6 U/mL. Geng et al¹¹ in their study assessed carcinogen antigen 125 (CA125) in saliva of OSCC patients. The saliva CA125 was significantly higher in patients with OSCC

(498.10±125.49 U/mL) than in patients with nonneoplastic disease (139.26±125.49 U/mL) and healthy controls (137.12±124.58 U/mL). A non-significant difference existed between all groups ($P > 0.05$).

There were 42 (75%) males and 14 (25%) females in our study. The study by Geng et al¹¹ had 97 OSCC, 36 patients with nonneoplastic disease and 50 controls. Balan et al¹² conducted a study on 60 SCC and 60 healthy subjects. Zini et al¹³ also observed higher prevalence of males than females in their study. We can suggest that more number of males in our study could be due to the high habit of tobacco consumption in contrast to females.

Our study had maximum cases were presented in age group 30-40 years i.e. 25 (44.6%) and minimum in age group 20-30 years 7 (12.5%). Younus et al¹⁴ conducted study on 138 OSCC patients and 30 normal subjects and found 30-39 years age group (29.7%) to be mostly affected.

Our study demonstrated that common site was buccal mucosa in 57.1%, tongue in 26.7%, labial mucosa in 5.3%, alveolar ridge in 5.3%, palate in 3.6% and lips in 1.8% cases. Younus et al¹⁴ found that in 58.0% cases Buccal mucosa was the commonest site. A study by Balan et al¹² showed buccal mucosa (24), tongue in 14, palate in 8, labial mucosa in 6, floor of the mouth and alveolar ridge in 4 each the most common sites of OSCC.

We found that our patients found to be 10 (17.8%) well differentiated, 26 (46.4%) in moderately differentiated and 20 (35.7%) poorly differentiated. It was seen that most of the patients i.e. 17 (30.3%) had stage IV, stage I was in 8 (14.2%), II in 11 (19.4%) and stage III was seen in 20 (35.7%) cases. Younus et al¹⁴ found that 37% had stage III and 40% had stage IV.

Higher salivary CA 125 level (520.5±168.4 U/mL) was observed in stage IV in our study and in poorly differentiated SCC (514.2±132.6 U/mL). Our results are in consistency with the results by Younus et al¹⁴ where a value of 593.1±57.15 U/mL and 597.2 ±60.5 U/mL were found respectively. Alamgir et al¹⁵ found significantly higher salivary CA125 level in OSCC patients than normal individuals and a statistically significant difference was observed among different histopathological grades as detected by ELISA.

The usefulness of saliva as a biological marker has been substantiated by various studies.^{16,17} The diagnosis value of saliva in oral diseases and cancers is well established. The readily availability, non-invasiveness makes saliva the best option. Bast and Colleagues first recognised CA 125 as a transmembrane mucin. It has also been found as a marker in ovarian and breast cancers.^{18,19,20,21}

There are few limitations of our study such as the diagnostic ability (Sensitivity/ specificity) of CA- 125 was not assessed. Moreover, the effect of age on level of CA- 125 was not detected.

CONCLUSION

Within the limitations of the study, we conclude that patients with OSCC had higher salivary CA- 125 level as compared to healthy control. Poorly differentiated SCC, cases of buccal mucosa and stage IV exhibited higher values.

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