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Original Research

Estimation of Salivary Biomarkers in patients with Squamous Cell Carcinoma

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ABSTRACT:

Background: Squamous cell carcinoma (SCC) accounts for nearly 90% cases of malignancy of oral cavity. The present study was conducted to assess the discriminatory salivary transcriptomic markers IL1b, IL8, SAT1, OAZ1 and 2 proteomic markers IL8 and IL1b in saliva of SCC patients. **Materials & Methods:** The present study was conducted on 94 SCC patients of both genders. Unstimulated whole saliva was collected and the saliva sample was centrifuged at 3000 rpm for 15 min to remove squamous cells and debris. Assessment of IL1b, IL8, SAT1, OAZ1 was done with PCR and LDH with standard kit method. **Results:** Out of 94 SCC patients, males were 56 and females were 38. IL 1 b level was 102.2 in group I and 24.5 in group II, IL 8 was 227. 8 in group I and 28 1 in group II, SAT 1 was 27.1 in group I and 23.1 in group II, OAZ1 was 23.6 in group I and 13.5 in group II, LDH level was 415.2 in group I and 124.5 in group II. The difference was significant (P< 0.05). **Conclusion:** Authors found elevated level of all salivary biomarkers in saliva of SCC patients as compared to healthy subjects. Thus saliva can act as a diagnostic tool.

Key words: Proteomic markers, Salivary biomarkers, squamous cells carcinoma

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INTRODUCTION

Oral cancer is the sixth most prevalent cancer worldwide. In the Indian subcontinent, it ranks among the three most common types of cancer.¹ Squamous cell carcinoma (SCC) accounts for nearly 90% cases of malignancy of oral cavity. The history of oral cancer shows that it is preceded in more than 70% of the patients by a recognized premalignant lesion (PML) and intervention at this stage may result in regression of the lesion.²

Oral squamous cell carcinoma (OSCC) is the most common cancer of the head and neck region. High morbidity and mortality is associated with this disease, but little improvement has been observed in the 5-year survival rate for patients with OSCC along the years.

One of the main prognostic factors for OSCC patients is advanced disease. Considering that, early diagnosis of oral cancer is an important approach to decrease morbidity and mortality rate.³

Saliva has been considered an important source of biologic information for the detection of human diseases. Beyond the obvious relationship with the oral mucosa surface, several studies have demonstrated synergism between the expression of molecular markers in saliva and systemic or distant sites diseases.⁴ Metabolites, proteins, coding and noncoding RNAs, and DNA have been detected in saliva of diseased patients, showing important value in disease detection. Saliva contains various biomarkers that help in detection of SCC.⁵ The present study was conducted to assess the

discriminatory salivary transcriptomic markers IL1b, IL8, SAT1, OAZ1 and 2 proteomic markers IL8 and IL1b in saliva of SCC patients.

MATERIALS & METHODS

The present study was conducted to in the department of General pathology. It comprised of 94 SCC patients of both genders. Equal number of controls was also included. The study protocol was approved from institutional ethical committee.

Data such as age, gender etc. was recorded in performa. Subjects were divided into 2 groups. Group I comprised

of 94 SCC patients and group II had 94 controls. All subjects were subjected to saliva collection. Unstimulated whole saliva was collected and the saliva sample was centrifuged at 3000 rpm for 15 min to remove squamous cells and debris. The resulting supernatant was used for further biochemical analysis. Assessment of IL1b, IL8, SAT1, OAZ1 was done with PCR and LDH with standard kit method. Results thus obtained were subjected to statistical analysis. P value less than 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Total- 94		
Gender	Males	Females
Number	56	38

Table I shows that out of 94 SCC patients, males were 56 and females were 38.

Graph I Distribution of patients

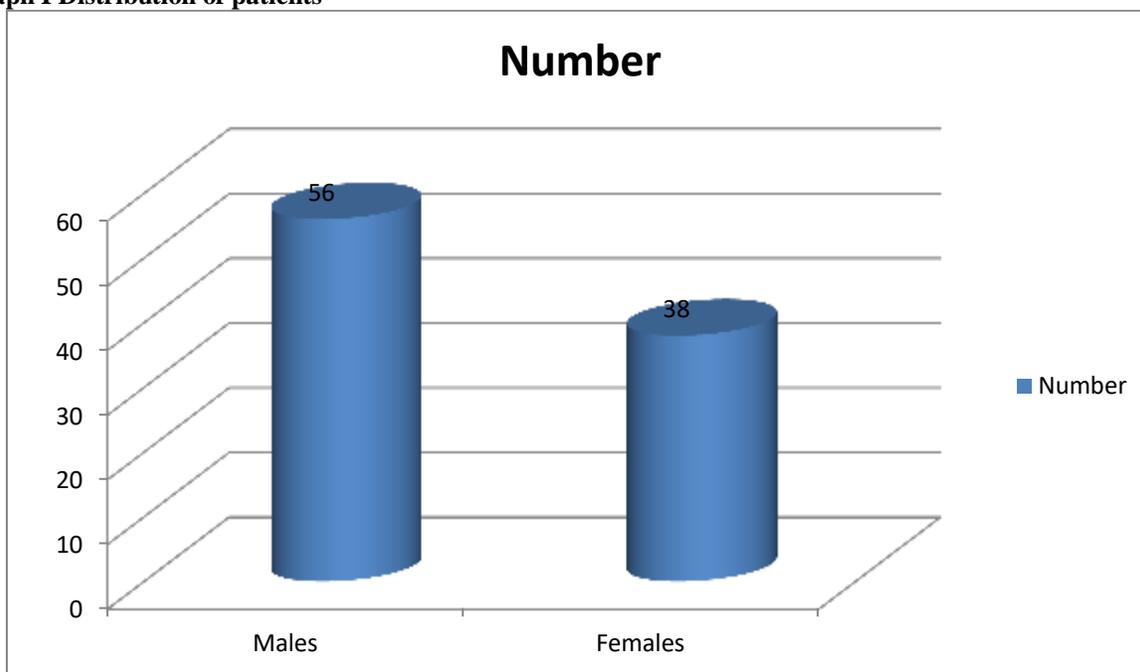
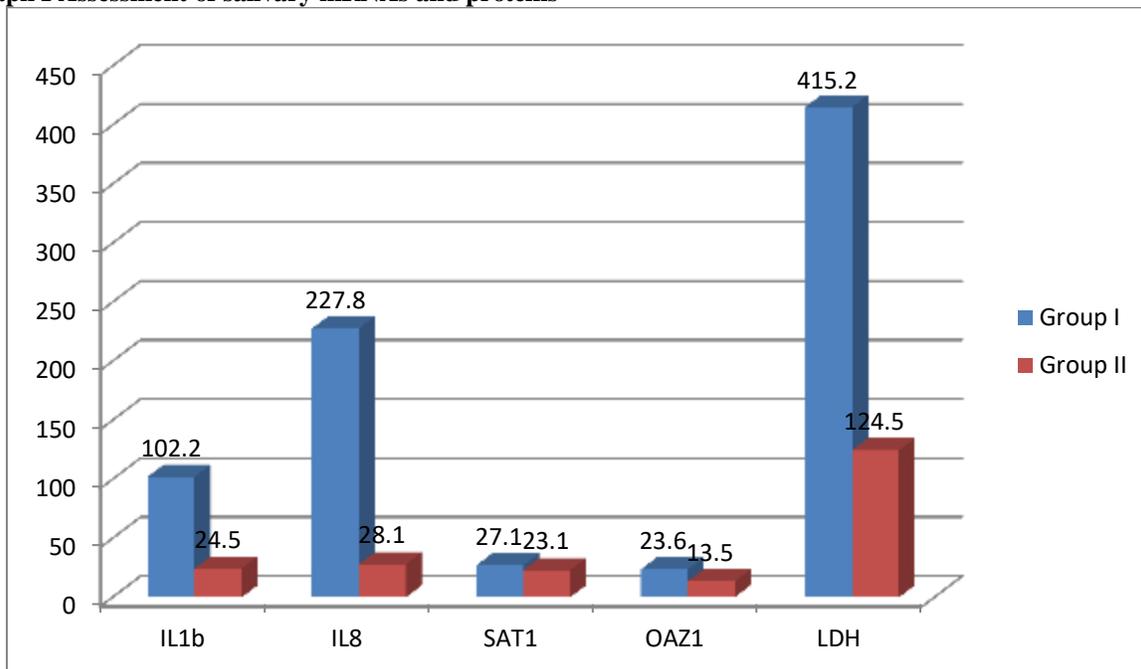


Table II Assessment of salivary mRNAs and proteins

Variable	Group I	Group II	P value
IL1b	102.2	24.5	0.01
IL8	227.8	28.1	0.001
SAT1	27.1	23.1	0.42
OAZ1	23.6	13.5	0.05
LDH	415.2	124.5	0.001

Table II, graph II shows that IL 1 b level was 102.2 in group I and 24.5 in group II, IL 8 was 227. 8 in group I and 28 1 in group II, SAT 1 was 27.1 in group I and 23.1 in group II, OAZ1 was 23.6 in group I and 13.5 in group II, LDH level was 415.2 in group I and 124.5 in group II. The difference was significant (P< 0.05).

Graph I Assessment of salivary mRNAs and proteins



DISCUSSION

Saliva is a multi-constituent oral fluid capable of mirroring both oral and systemic health conditions.⁶ Salivary analysis has been shown to be a useful diagnostic tool for other distant malignancies, including breast cancer, lung cancer, Sjogren syndrome, and pancreatic cancer. Saliva contains biomarkers, which can be used as indicators of disease.⁷ According to the National Institutes of Health (NIH), a biomarker is a characteristic that is objectively measured and evaluated as an indicator of a normal biological process, pathogenic process, or pharmaceutical response to therapeutic intervention. A biomarker must be verified and validated before it can be used in a clinical assay and have any impact or application in health risk assessment.⁸ The present study was conducted to assess the discriminatory salivary transcriptomic markers IL1b, IL8, SAT1, OAZ1 and 2 proteomic markers IL8 and IL1b in saliva of SCC patients.

In present study, out of 94 SCC patients, males were 56 and females were 38. Li et al⁹ found that a total of 180 samples (60 OSCC patients, 60 controls, and 60 PMOD patients) were used in the study. Seven transcriptomic markers (IL8, IL1b, SAT1, OAZ1, DUSP1, S100P, and H3F3A) were measured using qPCR, and two proteomic markers (IL8 and IL1b) were evaluated by ELISA. Among 7 transcriptomic markers, transcript level of DUSP1 was significantly lower in OSCC

patients than in controls and PMOD patients. Between the proteomic markers, the protein concentration of IL8 and IL1b was significantly higher in OSCC patients than controls and dysplasia patients. Univariate fractional polynomial (FP) models revealed that salivary IL8 protein (IL8p) has the highest AUC value between OSCC patients and controls (0.74) and between OSCC and PMOD patients (0.72). Applying a 2-marker FP model, salivary IL8p combined with IL1b gave the best AUC value for discrimination between OSCC patients and controls, as well as the IL8p combined with H3F3AmRNA, which gave the best AUC value for discrimination between OSCC and PMOD patients. Multivariate models analysis combining salivary analytes and risk factor exposure related to oral carcinogenesis formed the best combinatory variables for differentiation between OSCC versus PMOL (AUC ¼ 0.80), OSCC versus controls (AUC ¼ 0.87), and PMOD versus controls (AUC ¼ 0.78).

We found that IL 1 b level was 102.2 in group I and 24.5 in group II, IL 8 was 227. 8 in group I and 28 1 in group II, SAT 1 was 27.1 in group I and 23.1 in group II, OAZ1 was 23.6 in group I and 13.5 in group II, LDH level was 415.2 in group I and 124.5 in group II.

Singh et al¹⁰ included 62 cases of oral squamous cell carcinoma of both genders. Subjects were divided into 2 groups. Group I had SCC patients whereas group II had

control. Unstimulated whole saliva was collected and CYFRA 21-1 and CA19-9 were estimated by ELISA method while LDH level was assessed based on standard kit method. Out of 62 patients, males were 42 and females were 20. The mean salivary biomarkers levels of LDH in group I was 424.8 and 112.5 in group II, CA19-9 was 22.4 in group I and 20.5 in group II and CYFRA 21-1 was 18.5 in group I and 3.6 in group II. The difference was significant ($P < 0.05$).

CONCLUSION

Authors found elevated level of all salivary biomarkers in saliva of SCC patients as compared to healthy subjects. Thus saliva can act as a diagnostic tool.

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