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Research Article

Prognostic Significance of Preoperative Salivary and Serum Lactate Dehydrogenase in Oral Squamous Cell Carcinoma Patients

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Abstract

Introduction: The growth of cancer is linked with a high glycolytic activity with a shift from aerobic respiration to anaerobic glycolysis. Carcinogenesis has a remarkable influence on lactate dehydrogenase (LDH) and is used as a biomarker in various cancers.

Aims: The study intends to assess preoperative salivary and serum LDH in oral squamous cell carcinomas (OSCC) patients and to analyse its relation with clinicopathologic characteristics.

Settings and Design: A total of ninety participants (60 OSCCs and 30 healthy controls) were included in the study.

Material and Methods: Salivary and serum LDH were assessed using LDH assessment kit and Spectrophotometer.

Statistical Analysis: Chi-square test, Mann-Whitney U test, Kruskal-Wallis test, Pearson correlation test and Receiver operative curve analysis were applied.

Results: Raised salivary LDH (≥ 450 IU/L) was seen in 70% of OSCCs. Mean salivary LDH were significantly higher in patients than controls. The Mean LDH was significantly higher in OSCCs with bone involvement by local extension of tumor than without. Raised serum LDH (> 228 IU/L) was seen in 83% of OSCCs. Mean serum LDH were significantly higher in patients than controls. The mean LDH was significantly higher in patients with nodal metastasis than without. The mean salivary LDH was significantly higher than the serum LDH in the patients and showed a highly significant positive correlation.

Conclusion: Results infer that elevated levels of LDH might be a sign of disease progression. Outcome of the present analysis proposes that magnitude of LDH may be an indicator of tumor burden and extent of disease.

Keywords: Lactate Dehydrogenase; Salivary; Serum; Oral Squamous Cell Carcinoma; Clinicopathologic Characteristics

Introduction

Oral squamous cell carcinoma (OSCC) is the sixth most common human cancer that encompasses at least 90% of all oral malignancies, with a 5-year mortality rate of approximately 50% which has not changed significantly in more than 50 years, and a high rate of morbidity. The therapeutic modality currently offered to OSCC patients is based on staging and grading. Unfortunately, these predictors are subjective and relatively unreliable; as two tumours with identical staging and grading often behave very differently [1]. Most prognostic factors are obtained only by surgical exploration and a subsequent histologic examination. However, before surgery, there is no reliable, critical marker that provides accurate data regarding the likelihood of regional metastasis, postoperative adjuvant therapy, and prognosis [2]. Thus, there has been an ever-growing effort dedicated to the basic research of oral cancer, focusing on the identification of biological indicators for the diagnosis of its biological nature and aggressiveness [3].

Tumor markers in serum, tissue and other body fluids during neoplastic process are of clinical value in the management of patients with various body cancers. Among all the body fluids, blood has been the media of choice for the study of the biochemical markers by the medical community, but it does have some inherent disadvantages. However, a growing number of researchers are finding that saliva provides an easily available, non-invasive diagnostic medium for rapidly widening range of disease and clinical situations [4].

The enzyme lactate dehydrogenase (LDH) is found in the cells of almost all body tissues [4]. Its main function is to catalyze the oxidation of lactate to pyruvate. LDH is always confined within cell cytoplasm and becomes extracellular when a cell dies. So, its extracellular presence is always related to cell necrosis and tissue breakdown [5]. LDH is believed to vary according to the metabolic requirement of each tissue and alternation in LDH levels have been observed

during development, under changing biological conditions, and in response to pathological processes [4]. Carcinogenic changes have tremendous influence in increasing LDH activity. These carcinogenic changes may lead to decreased lactate to pyruvate conversion resulting in anomaly in the regeneration of nicotinamide adenine dinucleotide (NAD+) which may interfere with glycolysis part of carbohydrate metabolism. The development of cancer is associated with a high glycolytic activity with a shift from aerobic respiration to anaerobic glycolysis [6]. Malignant tumor tissue or contiguous tissue damaged by tumor liberates enzymes into circulation which contributes towards abnormal increase in enzyme levels [4,7]. Serum LDH levels have been used as a biochemical marker in diagnosis in various cancers like oral, laryngeal and breast cancer. It is a ubiquitous enzyme that plays a significant role in the clinical diagnosis of pathologic processes [8]. Serum and salivary LDH levels have not been studied rigorously in oral cancer and precancer [4]. Thus, the study is designed to assess preoperative salivary and serum LDH levels in OSCC patients and to analyse its relation with clinicopathologic characteristics (CPC).

Material and Methods

Ninety subjects ranging from 25 - 80 years were included in this hospital based case control study. Ethical clearance was obtained from the institutional review board (IRB No. 2014/OP/23) of our institution. After obtaining the informed consent from the participating subjects, a detailed Medical history, habit history and clinical details were recorded.

Group I consist of 60 untreated OSCC patients who underwent surgery in CFU of the institute (Excision of lesion along with neck dissection based on the clinical stage after the preoperative tumor survey). The patients were diagnosed based on clinical and histopathological examinations. Staging was according to the union for International Cancer Control Classification. Along with the complete blood investigations performed routinely prior to surgery, the patient's preoperative serum and salivary LDH was also elevated.

Clinicopathologic data

Clinical details like site, size of tumor, clinical stage, type of growth, associated with any potentially malignant disorders were collected during clinical examination. Imaging and gross specimen details were obtained from the investigations and gross examination of the surgically excised specimen. Paraffin sections for the analysis of histopathological features were obtained from the surgical excised tissue specimen. The selected hematoxylin and eosin stained slide were assigned with random numbers and the observers were blinded to the lymph node status. The order in which the cases were examined was randomized.

Group II consist of thirty, age and sex matched healthy individuals registered for a routine dental check-up and treatment in our institution. These participants were without any oral lesions and had no history of tobacco/areca nut products and alcohol use. These were randomly selected from the subjects visiting the outpatient department. All these participants had similar socioeconomic position and diet to OSCC patients.

Exclusion criteria

Patients suffering from systemic conditions like cardiovascular disease, anemia, liver, kidney and pancreatic diseases, blood dyscrasias, stroke, muscular dystrophy and autoimmune diseases were excluded. Patients with concurrent acute inflammatory disease, other mucosal lesions and medications were not enrolled. OSCC patients with cancer at other sites, OSCC patients with preoperative chemotherapy or radiotherapy, patients with only local resection without neck dissection and patients with recurrence were not included.

Method for LDH estimation (Saliva/Serum)

3ml of unstimulated whole saliva was collected from each of these patients by spit method in the calibrated measuring cup. Care was taken to see that patients does not consume food, smoke or chew gum at least one hour before the saliva collection procedure. Saliva was immediately centrifuged at 2500 rpm for 10 min to remove cells and debris. The resulting supernatant was separated into aliquots and subjected for analysis.

Under all aseptic precautions about 5 ml fasting venous blood was collected from antecubital vein of study and control group into plain sterile bulb. The sample is then allowed to clot at room temperature and then centrifuged at 3000 rpm for 10 minutes, to separate the serum. Unhemolysed serum samples were collected.

Both salivary and serum LDH levels was measured using biochemistry analyzer (Spectrophotometer EM 360; Erba Diagnostics, Mannheim, Germany) with cell holder thermo stable at 37°C, along with a commercially available LDH assessment kit. LDH catalyzes the oxidation of lactate by NAD+, to form pyruvate and NADH. The catalytic concentration is determined from the rate of increase of NADH, measured at 340nm. Reference range: 132-228 U/L at 37°C (Serum).

Statistical analysis

The data were analyzed by means of SPSS - 20. software (SPSS Inc., Chicago, IL, USA). The data are presented as means ± standard deviations and percentages. Mann-Whitney U test, Kruskal-Wallis, Chi-square test, Pearson correlation coefficient and Receiver operating characteristics (ROC) curve analysis were used. A p-value of < 0.05 was considered to indicate statistical significance.

Results

The CPC of the 60 OSCC patients are shown in table 1. The preoperative salivary LDH ranged from 103-3557 IU/L with the mean value of 1143.70 ± 749.53 IU/L in OSCC patients. Raised LDH (≥ 450 IU/L) was seen in 70% (42/60) of OSCC patients. Mean salivary LDH level were significantly higher in OSCC patients compared to controls (1143.70 ± 749.53 vs 268.23 ± 67.84) ($p = 0.000$) The salivary median activity value of LDH in the healthy control group was 271 IU/L and 285% higher in the cancer patients.

Parameters	Category	Total (%)	LDH IU/L		Chi-square	p-Value	Significance
			Negative (< 450) No%	Positive (≥ 450) No%			
Age	< 45 ≥ 45	22 (37%) 38 (63%)	5 (23%) 13 (34%)	17 (77%) 25 (66%)	0.875	0.350	NS
Gender	Male Female	51 (85%) 9 (15%)	17 (33%) 1 (12%)	34 (67%) 8 (88%)	1.799	0.180	NS
Site	BM, RMT Others	31 (52%) 29 (48%)	9 (29%) 9 (31%)	22 (71%) 20 (69%)	0.029	0.866	NS
Habits	PTC CH	42 (70%) 18 (30%)	14 (33%) 4 (22%)	28 (67%) 14 (78%)	0.741	0.389	NS
Duration of Habits	≤15 yrs >15yrs	29 (48%) 31 (52%)	7 (24%) 11 (35%)	22 (76%) 20 (65%)	0.918	0.338	NS
Tumor Size	T 1+2 T 3+4	26 (43%) 34 (57%)	10 (38%) 8 (23%)	16 (62%) 26 (77%)	1.564	0.211	NS
Tumor Stage	Early Advanced	17 (28%) 43 (72%)	7 (41%) 11 (26%)	10 (59%) 32 (74%)	1.411	0.235	NS
Tumor Depth (Imaging)	< 15 mm ≥ 15 mm	27 (45%) 33 (55%)	8 (30%) 10 (31%)	19 (70%) 23 (69%)	0.003	0.955	NS
Lymph Node Metastasis	N0 N+	25 (42%) 35 (58%)	8 (32%) 10 (29%)	17 (68%) 25 (71%)	0.082	0.775	NS
Bone Involvement	Absent Present	41 (68%) 19 (32%)	17 (41%) 1 (5%)	24 (59%) 18 (95%)	8.102	0.004	**S**
Skin Involvement	No Yes	51 (85%) 9 (15%)	15 (29%) 3 (33%)	36 (71%) 6 (67%)	0.560	0.813	NS
Broders Grade	Well Moderate Poor	29 (48%) 16 (27%) 15 (25%)	11 (38%) 5 (31%) 2 (13%)	18 (62%) 11 (69%) 13 (87%)	2.865	0.239	NS
Ifg (Tms)	4-8 9-12 13-16	13 (22%) 15 (25%) 32 (53%)	5 (38%) 3 (20%) 10 (31%)	8 (62%) 12 (80%) 22 (69%)	1.181	0.554	NS
Eosinophils	Present Absent	20 (33%) 40 (67%)	5 (25%) 13 (32%)	15 (75%) 27 (68%)	0.357	0.550	NS
Tumor Stromal Border	Infiltrative Pushing Mixed	34 (57%) 18 (30%) 8 (13%)	13 (38%) 4 (22%) 1 (12%)	21 (62%) 14 (78%) 7 (88%)	2.783	0.249	NS
Perineural Invasion	Present Absent	14 (23%) 46 (77%)	5 (35%) 13 (28%)	9 (65%) 33 (72%)	0.284	0.594	NS
Tumor Budding	Present Absent	40 (67%) 20 (33%)	12 (30%) 6 (30%)	28 (70%) 14 (70%)	0.000	1.000	NS

Table 1: The association between preoperative salivary LDH and clinicopathologic characteristics of OSCC patients (N = 60).

PTC: Pan Tobacco Chewers; CH: Combination of Habits; BM: Buccal Mucosa; RMT: Retromolar Trigone; others, includes lip, tongue and floor of mouth; T1+2 < 4 cms; T3+4 > 4 cms; N_0: Negative; N_+: Positive; IFG; Invasive Front Grading; TMS: Total Malignancy Score.

When compared with all the CPC, salivary LDH revealed an association only with BI (p = 0.004) (Table 1). The Mean LDH was significantly higher in OSCC cases with BI than without (1466.21 ± 842.65 vs 994.24 ± 660.92) (p = 0.044).

ROC curve analysis was used to evaluate the cut-off, sensitivity, and specificity values. The ROC was used to determine the best LDH value that yielded the optimal predictive value for determining BI. Figure 1 shows ROC curve for the Salivary LDH used to make the clinical decision regarding BI. The area under the ROC was 0.663.

The best cut-off values for predicting BI was 571.5 U/L for the Salivary LDH with 94.7% sensitivity and 41.5% specificity (p = 0.044) (Table 2).

Variable	Cut-off-value (IU/L)	Sensitivity (%)	Specificity (%)	AUC (%)	p-value
Salivary LDH	571.5	94.7	41.5	66.3	0.044

Table 2: Area under the curve and cut-off values obtained by ROC curve analysis.

AUC: Area Under the Curve; LDH: Lactate Dehydrogenase.

Figure 1: ROC curve for the salivary LDH used to make the clinical decision regarding BI.

The pre-operative serum LDH levels ranged from 41 - 1929 IU/L with the mean value of 533.05 ± 344.03IU/L in OSCC patients. Raised LDH (> 228 IU/L) was seen in 83% (50/60) of OSCC patients. Mean serum LDH levels were significantly higher in OSCC patients compared to controls (533.05 ± 344.03 vs174.46 ± 46.48) (p = 0.000) The serum median activity value of LDH in the healthy control group was 165.5 IU/L and 205% higher in the OSCC patients.

When compared with all the CPC, serum LDH revealed an association with LNM (p = 0.046). The mean LDH was significantly higher in OSCC patients with LNM than without (614.20 ± 367.36 vs 419.44 ± 277.01) (p = 0.036) (Table 3), The ROC was used to determine the best LDH value that yielded the optimal predictive value for determining LNM. Figure 2 shows ROC curve for the Serum LDH used to make the clinical decision regarding LNM. The area under the ROC was 0.660. The best cut-off values for predicting LNM was 238 U/L for the Serum LDH with 91.4% sensitivity and 36% specificity (p = 0.036) (Table 4).

Figure 2: RROC curve for the serum LDH used to make the clinical decision regarding LNM.

The mean LDH was significantly higher in OSCC cases with the combination of habits than with the pan tobacco chewing (707.27 ± 436.02 vs 458.38 ± 269.18) (p=0.042). The mean LDH was significantly higher in poorly differentiated tumors than with well differentiated tumors (590.21 ± 390.29 vs 341.53 ± 245.98). Similarly, LDH was significantly higher in moderately differentiated tumors than with well differentiated. (577.06 ± 257.01 vs 341.53 ± 245.98) (p = 0.035) (Table 3).

The mean salivary LDH was significantly higher than the mean serum LDH in the OSCC patients (1143.70 ± 749.53 vs 533.05 ± 344.03) (p = 0.000) The salivary median activity value in cancer patient group was 1046 IU/L. The serum median activity value in cancer patients group was 505 IU/L. Salivary median activity value is 107% higher than the serum median activity in the cancer patient group. The Pearson correlation coefficient was 0.524 and corresponding p = 0.000, a highly significant positive correlation between salivary and serum LDH in OSCC patients were noted.

Parameters	Category	Total (N)	OSCC Serum LDH IU/L (Mean ± SD)	p-value	Significance
Age	< 45 yrs ≥ 45 yrs	22 38	499.81 ± 284.97 552.28 ± 376.31	0.957	NS
Gender	Male Female	51 9	499.81 ± 284.97 552.28 ± 376.31	0.508	NS
Site	BM, RMT Others	31 29	491.58 ± 232.58 577.37 ± 433.02	0.446	NS
Habits	PTC CH	42 18	458.38 ± 269.18 707.27 ± 436.02	0.042	S
Duration of Habits	≤ 15 yrs > 15yrs	29 31	479.48 ± 277.15 583.16 ± 394.61	0.487	NS
Tumor Size	T 1+2 T 3+4	26 34	565.61 ± 414.23 508.14 ± 283.10	0.988	NS
Tumor Stage	Early Advanced	17 43	452.11 ± 293.13 565.04 ± 360.33	0.286	NS
Tumor Depth (Imaging)	< 15mm ≥ 15mm	27 33	555.37 ± 308.63 514.78 ± 374.37	0.523	NS
Broders Grade	Well Moderate Poor	29 16 15	479.68 ± 323.11 661.75 ± 430.78 498.93 ± 255.16	0.219	NS*
Ifg (Tms)	4-8 9-12 13-16	13 15 32	341.53 ± 245.98 577.06 ± 257.01 590.21 ± 390.29	0.035	S*
Lymph Node Metastasis	N0 N+	25 35	419.44 ± 277.01 614.20 ± 367.36	0.036	S
Bone Involvement	No Yes	41 19	516.04 ± 297.44 569.73 ± 435.06	0.918	NS
Tumor Stromal Border	Infiltrative Pushing Mixed	34 18 8	526.55 ± 269.59 565.66 ± 472.52 487.25 ± 327.75	0.868	NS*
Perineural Invasion	Present Absent	14 46	605.35 ± 472.11 511.04 ± 297.78	0.594	NS
Tumor Budding	Present Absent	40 20	551.12 ± 351.62 496.90 ± 334.21	0.490	NS
Tumor Thickness	< 6 > 6	14 46	512.00 ± 262.93 539.45 ± 367.47	0.986	NS

Table 3: Relationship between serum LDH and clinicopathologic characteristics in patients with OSCC. PTC: Pan Tobacco Chewers; CH: Combination of Habits; BM: Buccal Mucosa; RMT: Retromolar Trigone; others, includes lip, tongue and floor of mouth; T1+2 < 4 cms; T3+4 > 4 cms; N0: Negative; N+: Positive; IFG: Invasive Front Grading; TMS: Total Malignancy Score.

Mann-Whitney U Test; * Kruskal-Wallis test

Variable	Cut-off-value (IU/L)	Sensitivity (%)	Specificity (%)	AUC (%)	p-value
Serum LDH	238	91.4	36	66	0.036

Table 4: Area under the curve and cut-off values obtained by ROC curve analysis.

AUC: Area Under the Curve; LDH: Lactate dehydrogenase.

Discussion

The LDH in the whole saliva within the oral cavity may originate from various sources because whole saliva is a combination of secretions. Nagler., *et al*. concluded that major source for whole saliva LDH is non-glandular and oral epithelium being the major source [8]; The major compositional difference between serum and saliva is that saliva is not a passive ultrafiltrate of serum and that salivary constituents may play a distinct physiological role. The profile of salivary LDH is entirely different from that found in plasma but is similar to that found in oral epithelium. This indicates that the major source of salivary LDH is probably the oral epithelium shedding cells and it is logical to assume that pathological alterations of oral epithelium like dysplasia or cancer may result in alteration of LDH profile in saliva. Therefore, salivary LDH may be evaluated for possible oral mucosal pathologies in a manner similar to that used for evaluating other tissue pathologies–such as those in heart, muscle, or liver for LDH detection in plasma [8,9]. Thus, LDH concentration in saliva, as an expression of cellular necrosis, could be a specific indicator for oral lesions that affect the integrity of the oral mucosa. There are several studies performed to estimate the LDH levels in serum of while its estimation in saliva is currently being explored [10].

In the present investigation, the highest value of salivary LDH obtained among the OSCC patients was 3557 IU/L and lowest value obtained was 103 IU/L. The mean salivary LDH were significantly higher in OSCC patients compared to controls. Similar findings were illustrated by several researchers [1,6,7,9-13]. Out of 60 OSCC patients, 42 had elevated pre-operative salivary LDH. The salivary median activity of LDH in OSCC group was 1046 IU/L and in the healthy was 271 IU/L and is 285% higher in the cancer patients. Following are the probable reasons for increase in LDH activity in cancer patients: Abnormal elevation in salivary biochemical findings in OSCC represents a release from pathologically altered cells rather than an increased biosynthesis caused by the leakage from interstitial fluids through the torn, damaged oral mucosa and gingival sulci [14]. Malignant tumor tissue or contiguous tissue damaged by tumor liberates enzymes into circulation which contributes towards abnormal increase in enzyme levels; Cell death and tissue destruction [6,15]. Main reason for increased LDH levels is mainly due to increased mitotic index and increased production of lactic acid by tumor cells. Increase of LDH level is mainly due to breakdown of glycoprotein into lactic acid formation [9].

Upregulation of glycolysis, uncoupling of glucose from OXPHOS and repression of OXPHOS facilitating tumor evolution [16]. Metabolic phenotype benefit cancer cells by avoiding generation of OXPHOS by electron transport chain [17]. Metabolic adaptability of cancer cells [16,18]. Hypoxia promotes transcription of LDHA by HIF-1 and upregulation of LDHA causes lactate production and decreased pH [16,17]. Hypoxia induces the expression of LDHA gene which encodes the LDH-5 isoform, the key player in reprogramming tumor metabolism to aerobic glycolysis or Warburg effect [16]. Thus, LDH may be an indicator of both tumor progression and activation of key oncogenic pathways [19].

Several studies found that LDH values significantly correlated with the histopathological grade of the tumor [6,7,9,13,16]. Hence, salivary LDH can be used to assess the aggressiveness of different histological grades of OSCC. In the present investigation despite of the fact that the mean salivary LDH increased with the different grades of OSCC but was statistically insignificant. The mean salivary LDH levels were higher in advanced stage tumors, tumors with LNM, tumors ≥ 15 mm in depth, in endophytic lesions, tumors with jaw BI and in poorly differentiated tumors compared to their counterparts, suggesting amplified salivary LDH production could be directly proportional to tumor volume, extent and degree of anaplasticity indicating an aggressive tumor type. As literature states about overexpression of LDH-5 have been found to promote invasive phenotype in oral and oesophageal squamous cell carcinomas [16,20,21].

Several investigators found that the serum level of LDH was significantly raised in malignancy group compared to control group [22-27]. Similar findings were observed in this study. The rationale for the rise in the level of serum LDH in malignancy: The fundamental alterations in cancer cell are the change from aerobic res-

piration to increased aerobic glycolysis and anaerobic glycolysis, i.e. fermentation. Malignant cell does not show normal Pasteur Effect but instead a high rate of glycolysis, and lactic acid production continues even in the presence of adequate oxygen. According to Gerson and Silverman, protein synthesis and mitotic activity takes place at a greater rate in dysplastic epithelium, than in nondysplastic epithelium. Both protein synthesis and cell division are energy consuming process. The requirement for energy is thus greater in dysplastic epithelium and this may account for an increase in glycolysis [28].

There is good biologic rationale for LDH as a predictive test; however, the exact mechanism is not understood. LDH serum levels also reflect cellular turnover by the tumor and enzyme release [19]. From the various hypothesis proposed by various workers, it is seen that three mechanisms may be responsible for the rise in the level of serum LDH. They can be necrosis and cellular degeneration; Induction process initiated by the tumor and involving normal tissues; Muscle degeneration caused by protein deficit [26,27]. For oral carcinomas, the initial 2 mechanism seems to be the most plausible [27].

There are many explanations for increasing LDH level in blood of patients suffering from cancer diseases. Following are: The increase number of cells during cancer development will consume great amount of glucose to get energy by glycolysis which increasing LDH level when the condition is anaerobic; Growing cancer cells will destroy other tissues and causing release of intracellular enzyme like LDH into the blood stream by the injury or dying cells; Increase LDH level by activating its production by tyrosine phosphorylation mechanism in cancer cells [29]. Genomic changes during malignant transformation; Increased LDH levels are due to increased mitotic index. More lactic acid production by tumor cells due to breakdown of glycoprotein [26]. LDH is greatly influenced by accidental hemolysis in serum therefore must be collected and transported with care [30]. LDH levels are increased in response to tissue injury, necrosis, hypoxia, hemolysis; Increased LDH activity may also reflect aberrant oncogene activity.

In this investigation when compared with all the CPC, serum LDH revealed a significant association with LNM. Results showed higher serum LDH values in OSCC patients with LNM than without LNM as the malignancy spreads, changes in blood are more striking than that in saliva while in local malignancy changes are more prominent in saliva than that in blood. Future investigations can focus on serum LDH activity in predicting LNM in OSCC patients. Khan., *et al.* [22]; Narang., *et al.* [24]; Liaw., *et al.* [30], found that serum LDH levels were significantly raised in metastatic group compared to non- metastatic group [22,24,30]. Mean serum LDH level differed significantly between grades of Bryne's invasive front grading. Pereira., *et al*. [26]; and Sharma., *et al*. [27] noted a raised level of LDH had a positive correlation with the histologic grading.

Conclusion

Serum and salivary LDH levels have not been studied rigorously in OSCC. Results revealed that salivary and serum LDH levels increase in OSCC in comparison to controls. Salivary and serum LDH estimation can be a valuable biochemical marker. Increase in LDH levels was consistent in saliva and serum of OSCC patients. The significant increase in salivary enzyme levels in patients with OSCC observed in this study validates the benefits of saliva measurement in comparison with serum assessment. Thus, this study proves the significance of saliva as a diagnostic tool especially in oral lesion such OSCC. Salivary LDH assessment can be an important alternative to serum LDH as a biochemical indicator, as it is unsophisticated, non-invasive method and is readily accepted by the patients.

Present analysis validates that there is an over expression of LDH in OSCC cases and also LDH has shown a relationship with few clinicopathologic characteristics. Outcome of the present analysis propose that magnitude of LDH may be an indicator of tumor burden and extent of disease. Results infer that elevated levels of LDH might be a prognostic sign of disease progression. Future analysis can focus on validation of serum LDH activity in predicting LNM. Further elaborated studies are required to prove the usefulness of salivary LDH in predicting aggressive phenotype. Future research involving large cohort of OSCC cases would underline the relationship between salivary LDH, LDH-5 and clinicopathologic characteristics more precisely.

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