SDM College of Dental Sciences & Hospital

QUANTIFICATION AND CLINICOPATHOLOGIC CORRELATION OF LACTATE DEHYDROGENASE AND C - REACTIVE PROTEIN IN ORAL SQUAMOUS CELL CARCINOMA PATIENTS

By **Dr. JYOTI KALE**

S.D.M. College of Dental Sciences LIBRARY t-1153 Sattur, Dharwad

Dissertation submitted to the
Rajiv Gandhi University of Health Sciences, Karnataka, Bangalore

In partial fulfillment
of the requirements for the degree of

MASTER OF DENTAL SURGERY (M.D.S.)

In

ORAL AND MAXILLOFACIAL PATHOLOGY & MICROBIOLOGY

Under the guidance of
Dr. SWETHA ACHARYA
DEPARTMENT OF ORAL AND MAXILLOFACIAL PATHOLOGY & MICROBIOLOGY

S.D.M. COLLEGE OF DENTAL SCIENCES & HOSPITAL, DHARWAD

APRIL 2017

Rajiv Gandhi University of Health Sciences, Karnataka, Bangalore

SDMCDSLRC
T-01153

Abstract

Background and Objectives:

The prognosis of oral squamous cell carcinoma (OSCC) is usually related to tumor stage and lymph node status. The response to radical therapy is not consistent. 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. 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. Lactate dehydrogenase (LDH) is one among such biomarkers. LDH is found in almost all the body cells. LDH catalyzes the final step in the metabolic chain of anaerobic glycolysis. LDH is one biomarker that can be obtained from serum as well as saliva. Salivary and serum LDH levels have not been studied comprehensively in OSCC. Thus, the study was designed to assess preoperative salivary and serum LDH levels in OSCC patients and to analyze its relation with clinicopathologic characteristics.

C-reactive protein (CRP) is an acute-phase protein and is synthesized in hepatocytes. CRP levels increase in a variety of infections, immuno-inflammatory diseases, trauma, and many types of cancers. Recently, there has been increasing evidence that a systemic inflammatory response is of prognostic value in various cancers. CRP is an index of systemic inflammation. Preoperative elevation of serum CRP has been reported to be a prognostic indicator in oesophageal, gastric, ovarian and colorectal carcinomas. However, CRP is not routinely measured preoperatively. Hence, the study intended to evaluate the preoperative serum CRP levels in OSCC patients and to analyze its relationship with the clinicopathologic characteristics.

Methods: A total of 90 participants (60 OSCC patients and 30 healthy controls) were included in the study. 60 clinically and histopathologically diagnosed cases of OSCC, who underwent surgical treatment in the Cranio-facial unit of S.D.M College of Dental Sciences and Hospital, Dharwad or in Karnatak Cancer Hospital and Research Centre, Hubli, were included and clinicopathological data was obtained.

3 ml of unstimulated whole saliva was collected from each of these patients by spit method in the calibrated measuring cup. Saliva was immediately centrifuged and 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 was then allowed to clot at room temperature and then centrifuged at 3000 rpm for 10 min, to separate the serum.

Both salivary and serum LDH levels were evaluated using commercially available LDH assessment kit and biochemistry analyzer.

CRP-Turbilatex is a quantitative turbidimetric test for the measurement of CRP in human serum. CRP level was evaluated using CRP assessment kit and biochemistry analyzer.

Evaluation of data and statistical analysis was carried out using Mann-Whitney U, Chi-square test and Receiver operating characteristics (ROC) curve analysis.

Results: The pre-operative salivary LDH levels ranged from 103-3557 IU/L with the mean value of 1143.70±749.53 IU/L in OSCC patients. Mean salivary LDH level

were significantly higher in OSCC patients compared to controls (1143.70±749.53 vs 268.23±67.84). Out of 60 OSCC patients, 42 patients had elevated pre-operative salivary LDH (≥450 IU/L), while18 had a normal salivary LDH value (<450 IU/L). Raised LDH was seen in 70% (42/60) of OSCC patients. When compared with all the clinicopathologic parameters, salivary LDH revealed an association only with bone involvement (BI) (p= 0.004). The mean LDH was significantly higher in OSCC cases with the BI than without (1466.21 ± 842.65 vs 994.24 ± 660.92) (p=0.044).

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. Mean serum LDH levels were significantly higher in OSCC patients compared to controls (533.05±344.03 vs 174.46±46.48). Out of 60 OSCC patients, 50 patients had elevated pre-operative serum LDH (>228IU/L) while 10 had a normal serum LDH value (130-228 IU/L). Raised LDH was seen in 83% (50/60) of OSCC patients. When compared with all the clinicopathologic parameters, serum LDH revealed an association with clinical nodal status (p= 0.046). The mean LDH was significantly higher in OSCC patients with involved clinical nodal status than without nodal involvement (614.20 ± 367.36 vs 419.44 ± 277.01) (p=0.036).

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 patient group was 505 IU/L. Salivary median activity value is 107% higher than the serum median activity in the cancer patient group.

The pre-operative serum CRP levels ranged from 0.3-86 mg/L with the mean value of 14.25±17.45 mg/L in OSCC patients. Mean CRP level was significantly higher in OSCC patients compared to controls (14.25±17.45 vs 2.68±1.32). Out of 60 OSCC patients, 42 patients had elevated pre-operative serum CRP levels while 18 had a normal serum CRP value (≤5mg/L). Raised CRP was seen in 70% (42/60) of OSCC patient. When compared with all the clinicopathologic parameters, CRP in OSCC patients were associated with clinical nodal status and lymph node metastasis (LNM) ($p<0.05$). Mean CRP was significantly higher in the lymph node metastatic group (N_+) than in the non-metastatic group (N_0)(21.29±22.17 vs 7.24±6.24)($p=0.000$). The area under the ROC curve analysis was 0.819. The best cut-off values for predicting LNM was 8.65mg/L for the CRP with 77% sensitivity and 77% specificity ($p<0.05$). CRP cut-off revealed a significant association with the LNM. The group having CRP >8.65 had higher number of cases with LNM (N_+) than in CRP ≤ 8.65group (77% vs 23%) ($p=0.000$).

Conclusion: Salivary and serum LDH levels increase in OSCC in comparison to controls. Increase in LDH levels was consistent in saliva and serum of OSCC patients. Results infer that elevated level of LDH might be a prognostic sign of disease progression. The results of the study suggest that both serum and saliva are reliable diagnostic tools. The significant increase in salivary LDH levels in OSCC patients observed in this study validates the benefits of salivary analysis in comparison with serum assessment.

Analysis confirms the relation between raised CRP and malignant potential of OSCC. The findings appear to support an association between the elevated preoperative CRP levels and LNM. Raised CRP may predict LNM. CRP might provide prognostic

information beyond that provided by cancer type, stage, and histology. Hence, CRP can be added as an extension to known clinicopathologic parameters to predict the prognosis in OSCC patients.

Key words: Oral Squamous Cell Carcinoma, lactate dehydrogenase, C –reactive protein, clinicopathologic parameters, Salivary LDH, Serum LDH