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Assessment of Matrix metalloproteinases (MMP) level in Oral Squamous Cell Carcinoma and Oral Leukoplakia

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ABSTRACT

Background: Matrix metalloproteinases (MMPs) are a family of enzymes that play a crucial role in the remodeling and degradation of extracellular matrix (ECM) components, such as collagen, elastin, and proteoglycans. The present study was conducted to assess MMP level in Oral Squamous Cell Carcinoma (OSCC) and Oral Leukoplakia (OL).

Materials & Methods: 40 clinically and histopathologically confirmed cases of OSCC and OL were enrolled. OSCC patients were included in group I. Patients diagnosed clinically with OL and showing various degrees of epithelial dysplasia histopathologically were included in group II. The group III included healthy subjects without any systemic illness. 1.5 ml of unstimulated saliva was obtained and the salivary MMP-9 level was measured using the quantitative sandwich enzyme-linked immunosorbent assay (ELISA) technique.

Results: Group I had 12 males and 8 females, group II had 13 males and 7 females and group III had 10 males and 10 females. The mean MMP-9 level in group I was 51.3 ng/ml, in group II was 32.8 ng/ml and in group III was 17.4 ng/ml. The difference was significant (P< 0.05). The salivary MMP-9 level in well differentiated grade was 48.6 ng/ml, in moderately differentiated grade was 47.2 ng/ml and in poorly differentiated grade was 64.9 ng/ml. The difference was significant (P< 0.05). The salivary MMP-9 level in mild dysplasia was 28.4 ng/ml, in moderate dysplasia was 31.5 ng/ml and in severe dysplasia was 39.8 ng/ml. The difference was significant (P< 0.05).

Conclusion: Salivary MMP-9 levels were higher in OL and OSCC patients than in healthy subjects. When comparing poorly differentiated OSCC to well and moderately differentiated OSCC, higher salivary MMP-9 levels were found. When comparing severe dysplasia to mild and moderate dysplasia, the mean salivary MMP-9 was greater.

Keywords: Matrix metalloproteinases, Dysplasia, Oral Leukoplakia, Oral Cancer

Introduction

Matrix metalloproteinases (MMPs) are a family of enzymes that play a crucial role in the remodeling and degradation of extracellular matrix (ECM) components, such as collagen, elastin, and proteoglycans.[1] They are involved in various physiological processes, including tissue remodeling, wound healing, and immune response, as well as pathological conditions such as inflammation, cancer, and cardiovascular disease.[2] In humans, the MMP family consists of more than 20 members, each with specific substrate preferences, cellular localization, and regulatory mechanisms.[3]

Matrix metalloproteinases (MMPs) have been implicated in the pathogenesis and progression of oral cancer (oral squamous cell carcinoma, OSCC). MMPs play a crucial role in tumor invasion and metastasis by degrading the extracellular matrix (ECM) components surrounding the tumor, allowing cancer cells to invade surrounding tissues and migrate to distant sites.[4] MMPs facilitate this process by cleaving ECM proteins such as collagen, laminin, and fibronectin. In OSCC, increased expression of MMPs, particularly MMP-2 and MMP-9, has been associated with enhanced invasion and metastasis. MMPs contribute to angiogenesis, the process of new blood vessel formation, which is essential for tumor growth and metastasis.[5] MMPs can degrade ECM proteins to facilitate the release of pro-angiogenic factors and promote the migration of endothelial cells. MMP-9, in particular, has been implicated in angiogenesis in OSCC, where increased expression of MMP-9 correlates with increased microvessel density and poor prognosis.[6] The present study was conducted to assess MMP level in oral squamous cell carcinoma (OSCC) and Oral leukoplakia (OL).

Materials & Methods

The present study was conducted on 40 clinically and histopathologically confirmed cases of OSCC and OL. All were informed regarding the study and their written consent was obtained. Data such as name, age, gender etc. was recorded. OSCC patients were included in group I. Patients diagnosed clinically with OL and showing various degrees of epithelial dysplasia histopathologically were included in group II. The group III included healthy subjects without any systemic illness. 1.5 ml of unstimulated saliva was obtained and the salivary MMP-9 level was measured using the quantitative sandwich enzyme-linked immunosorbent assay (ELISA) technique. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I Distribution of patients

Group	Group I (20)	Group II (20)	Group III (20)
M:F	12:8	13:7	10:10

Table I shows that group I had 12 males and 8 females, group II had 13 males and 7 females and group III had 10 males and 10 females.

Table II Salivary MMP-9 levels

Groups	Mean (ng/ml)	P value
Group I	51.3	0.01
Group II	32.8	

Group III	17.4	

Table II, graph I shows that mean MMP- 9 level in group I was 51.3 ng/ml, in group II was 32.8 ng/ml and in group III was 17.4 ng/ml. The difference was significant (P< 0.05).

Graph I Salivary MMP-9 levels

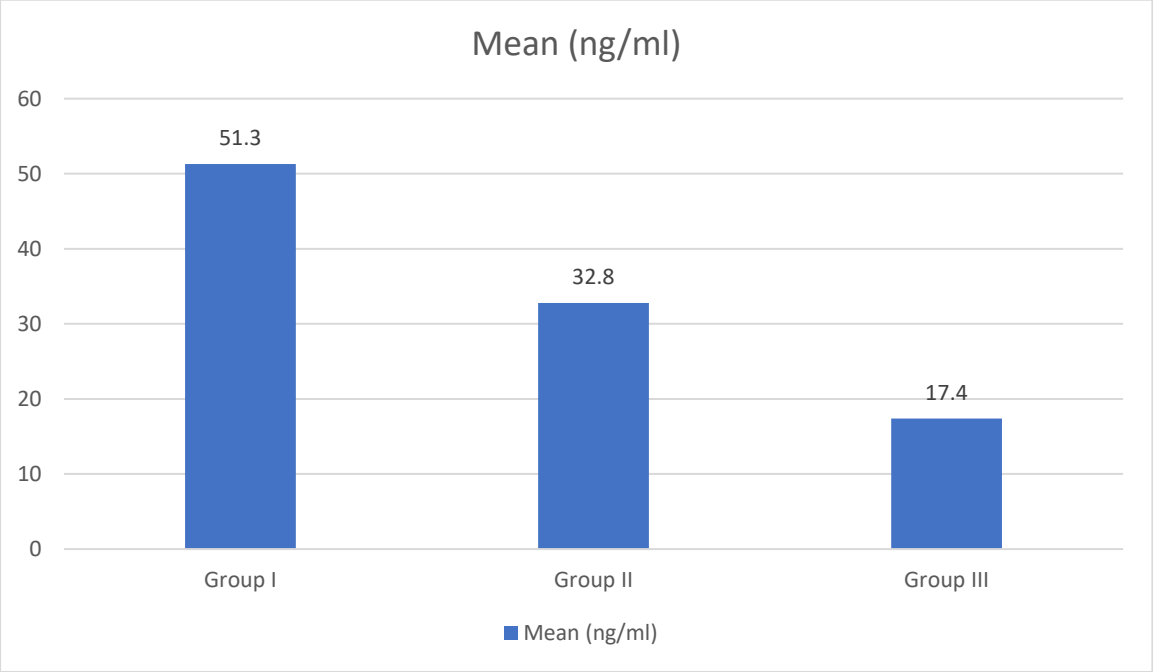

Table III Assessment of salivary MMP-9 levels in different histological grades of OSCC

Grade	Mean (ng/ml)	P value
Well differentiated	48.6	0.01
Moderately differentiated	47.2	
Poorly differentiated	64.9	

Table III shows that salivary MMP- 9 level in well differentiated grade was 48.6 ng/ml, in moderately differentiated grade was 47.2 ng/ml and in poorly differentiated grade was 64.9 ng/ml. The difference was significant (P< 0.05).

Table IV Assessment of salivary MMP-9 levels in different histological grades of oral epithelial dysplasia

Grade of dysplasia	Mean (ng/ml)	P value
Mild	28.4	0.04
Moderate	31.5	
Severe	39.8	

Table IV shows that salivary MMP- 9 level in mild dysplasia was 28.4 ng/ml, in moderate dysplasia was 31.5 ng/ml and in severe dysplasia was 39.8 ng/ml. The difference was significant (P< 0.05).

Discussion

By affecting immune cell infiltration and function as well as the structure and content of extracellular matrix (ECM) proteins, MMPs have an impact on the formation of the tumor microenvironment.[7] Tumor growth and progression can be facilitated by an inflammatory and immunosuppressive milieu that is fostered by dysregulation of MMP expression. Moreover, growth factors and cytokines implicated in the development and spread of tumors can be cleaved and activated by MMPs.[8,9] In patients with OSCC, elevated expression levels of MMPs, especially MMP-2 and MMP-9, have been linked to a poor prognosis and decreased survival. Higher tumor stages, more aggressive tumor behavior, and a higher risk of metastasis and recurrence are all correlated with increased MMP expression.[10] The present study was conducted to assess MMP level in Oral Squamous Cell Carcinoma (OSCC) and Oral Leukoplakia (OL).

We found that Group I had 12 males and 8 females, group II had 13 males and 7 females and group III had 10 males and 10 females. The mean MMP- 9 level in group I was 51.3 ng/ml, in group II was 32.8 ng/ml and in group III was 17.4 ng/ml. Pazhani J et al[11] evaluated the salivary levels of MMP-9 in OSCC and oral leukoplakia patients using enzyme-linked immunosorbent assay (ELISA) among 102 subjects, which included 34 OSCC patients (group I), 34 OL patients (group II), and 34 healthy subjects (group III). Unstimulated saliva was collected and the salivary MMP-9 was estimated in mg/ml using the sandwich ELISA technique. The mean salivary MMP-9 level in OSCC, OL, and normal oral mucosa was 50.9 ± 5.7 ng/ml, 31.6 ± 6 ng/ml, and 16.2 ± 4.8 ng/ml, respectively. Patients with OSCC had significantly higher levels of salivary MMP-9 when compared to OL and normal mucosa. Higher levels of salivary MMP-9 were observed in poorly differentiated OSCC when compared to well and moderately differentiated OSCCs. The salivary MMP-9 was higher in severe oral epithelial dysplasia when compared to mild and moderate oral epithelial dysplasia.

We observed that salivary MMP- 9 level in well differentiated grade was 48.6 ng/ml, in moderately differentiated grade was 47.2 ng/ml and in poorly differentiated grade was 64.9 ng/ml. Tondon et al[12] in their study histopathologically proven oral squamous cell carcinoma cases were collected. Among the different sites of oral cavity, the highest incidence (31.47%) of oral squamous cell carcinoma was seen for buccal mucosa in our study. The most affected age group (39.50%) were patients above 50 years old, predominantly involving males.

We observed that salivary MMP-9 level in mild dysplasia was 28.4 ng/ml, in moderate dysplasia was 31.5 ng/ml and in severe dysplasia was 39.8 ng/ml. Peisker A et al[13] study comprised 30 OSCC patients and 30 healthy controls in total. The control group's median absorbance MMP-9 value was 0.156 (IQR=0.102), while the OSCC group's was 0.186 (IQR=0.158). The OSCC patients had a considerably higher level of MMP-9 (+19.2%) compared to the controls (p=0.008). The median values for patients who experienced a primary event were 0.186 (IQR=0.134) and patients who experienced a recurrence were 0.233 (IQR=0.299), respectively. Patients with a primary incident had a substantial rise in MMP-9 (p=0.017) as compared to controls, by a margin of +19.2%. When recurrence patients and healthy controls were compared, there was no discernible rise in MMP-9 levels (+49.4%;

p=0.074). The degree of sensitivity of MMP-9 was 100% whereas the specificity value was 26.7% with AUC of 0.698.

The shortcoming of the study is small sample size.

Conclusion

Authors found that salivary MMP-9 levels were higher in OL and OSCC patients than in healthy subjects. When comparing poorly differentiated OSCC to well and moderately differentiated OSCC, higher salivary MMP-9 levels were found. When comparing severe dysplasia to mild and moderate dysplasia, the mean salivary MMP-9 was greater.

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