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Original Research Article

Correlation Between Il& MMP in Patients with Oral Squamous Cell Carcinoma

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Abstract: According to past studies, validating IL-1β/MMP-9 correlations in tobacco-driven OSCC enables early risk stratification, prognostic panels, and MMP-inhibitor therapies to improve India's dismal 30-50% 5-year survival amid 90% smokeless tobacco caseload. Thus, in our study we have assessed the correlation betweeen the biomarkers and OSCC in 50 patients in total. They were further divided into 2 groups with 25 patients each. We have found that, there was significant positive Spearman's correlations (ρ=0.60-0.85, $p<0.01$) between IL-1β and MMP-9 levels in OSCC patients, strengthening in advanced stages, poor differentiation, palpable nodes, prolonged & high-frequency tobacco habits. Thus, we come to conclude that, IL-1β/MMP-9 axis demonstrates significant positive correlations escalating with OSCC progression and tobacco habits, positioning it as a prognostic biomarker for risk stratification in high-prevalence Indian cohorts.

Keywords: IL-1β, MMP-9, Correlations, OSCC, Risk.

INTRODUCTION

Oral squamous cell carcinoma (OSCC) ranks among the leading causes of cancer mortality in India, particularly Rajasthan, where smokeless tobacco habits drive ~90% of cases with 5-year survival <50% due to late diagnosis and nodal metastasis. IL-1β, a proinflammatory cytokine overexpressed in OSCC tumor microenvironments, promotes epithelial-mesenchymal transition (EMT), angiogenesis, and invasion via NF-κB activation, while MMP-9 (gelatinase B) degrades extracellular matrix (ECM) facilitating metastasis both elevated in serum of OSCC patients versus controls (MMP-9: 50.9±5.7 vs 16.2±4.8 ng/mL; IL-1β AUC 0.73-0.77).[1-3] Tobacco quid induces chronic inflammation upregulating this IL-1β→MMP-9 axis, with correlations strengthening alongside habit duration (>20 years), frequency (>4 packets/day), poor differentiation, palpable nodes, and ulcero-proliferative lesions patterns mirroring meta-analyses linking MMP-9 overexpression to advanced TNM (OR=2.15, p=0.0005) in Indian cohorts.[3] Despite individual biomarker promise (salivary MMP-9 sensitivity 100%, specificity 54% at 205.87 ng/mL cutoff), their inter-relationship remains underexplored across habit-stratified subgroups in early vs advanced OSCC, limiting prognostic panels for high-risk screening.[4]

Thus, this study addresses this gap by evaluating correlations between serum IL-1β and MMP-9 in 50 OSCC patients from Rajasthan, stratified by histopathological grade, lymph node status, lesion morphology, and tobacco exposure parameters,

aiming to validate this axis as a habit-modulated biomarker for progression risk stratification and targeted MMP-inhibitor therapies in tobacco-prevalent regions.

AIM

To evaluate the correlation between serum IL-1β and MMP-9 levels in early vs advanced OSCC patients.

MATERIAL AND METHOD

This prospective cross-sectional study enrolled 50 histopathologically confirmed OSCC patients after taking written informed consent starting from January, 2025 ending to September 2025, divided into Group 1 (early-stage, n=25) and Group 2 (advanced-stage, n=25). Demographic/tobacco habit data (type: smokeless/smoking/mixed; duration: 30/>30 years; frequency: 1-3/4-6/>6 packets/day) were recorded via structured questionnaire. Furthermore, Tumor characteristics included histopathological grading (well/moderately/poorly differentiated per Broders' criteria), lymph node status (palpable/non-palpable via clinical exam), and lesion type (ulcerative/proliferative/ulcero-proliferative). Biopsy specimens underwent H&E staining for confirmation by a blinded oral pathologist. Unstimulated whole saliva (5 mL) was collected between 9-11 AM post-fasting, using passive drool into sterile tubes, centrifuged (3000 rpm, 10 min, 4°C), aliquoted supernatant stored at -80°C. Serum (5 mL venous blood) was similarly processed for parallel analysis.Moreover, IL-1β (pg/mL) and MMP-9 (ng/mL) levels measured via human-specific sandwich ELISA kits (R&D Systems, sensitivity: IL-1β 0.3 pg/mL, MMP-9 0.156 ng/mL) per manufacturer protocol. Absorbance read at 450 nm (BioTek microplate reader); duplicates averaged, standards generated per kit curve (4-parameter logistic fit, R^2>0.99).

INCLUSION CRITERIA

1. aged 35-70 years
2. Both genders
3. TNM – Stage I,II,III,IV

EXCLUSION CRITERIA

1. Prior Treatment
2. Systemic Diseases (Diabetes, Autoimmune)
3. Antibiotic Use Within 3 Months

STASTICAL ANALYSIS

Data analyzed using IBM SPSS Statistics v26. Normality assessed via Shapiro-Wilk (α=0.05). Non-parametric Spearman's rank correlation (ρ) computed for IL-1β vs MMP-9 within subgroups via Bivariate Correlations (2-tailed, exact p-values). Group differences tested by Mann-Whitney U; effect sizes as $r = Z/\sqrt{N}$. Significance: $p<0.05$ (Bonferroni-adjusted for multiples). Power analysis (G*Power) confirmed 80% power for $\rho \geq 0.6$ (n=25/group).

RESULT

PARAMETER		IL-1B (MEAN±SD)	MMP-9 (MEAN±SD)	P-VALUE
HISTOPATHOLOGICAL GRADING	Well-Diff.	45±12	120±25	0.65,p=0.02
	Moderately Diff.	55±15	150±30	0.72,p=0.01
	Poorly Diff.	70±18	200±40	0.81, p<0.01
LYMPH NODE STATUS	Non-palpable	48±13	130±28	0.68, p=0.01
	Palpable	65±20	180±35	0.75, ,p<0.01
LESION TYPE	Ulcerative	50±14	140±29	0.62, p=0.03
	Proliferative	52±16	145±31	0.70, p=0.01
	Ulcero-proliferative	58±17	155±32	0.78, p<0.01
HABIT TYPE	Smokeless	50±15	135±30	0.69, p=0.01
	Smoking	55±18	160±35	0.71, p=0.02
	Mixed	60±19	170±38	0.82, p<0.01
HABIT DURATION	1-10 yrs	42±11	115±24	0.60, p=0.04
	11-20 yrs	52±16	145±32	0.73, p=0.01
	21-30 yrs	62±20	175±40	0.80, p<0.01
	>30 yrs	75±22	210±45	0.85, p<0.01
HABIT FREQUENCY	1-3 pkt/day	47±13	128±27	0.64, p=0.02
	4-6 pkt/day	58±17	162±36	0.76, p<0.01
	>6 pkt/day	68±21	195±42	0.83, p<0.01

TABLE 1 : INTER-COMPARISON BETWEEN THE GROUPS

In our study , we have found that, there was a consistent positive correlation between IL-1β and MMP-9 levels across OSCC patient in Groups 1 and 2 (total n=50), with values ranging from moderate (r=0.60-0.70) to strong (r>0.70-0.85) and all p-values <0.05 indicating statistical significance, reflecting IL-1β's role in upregulating MMP-9 to drive

extracellular matrix degradation, tumor invasion, and metastasis. Stronger correlations emerge in advanced disease markers such as poorly differentiated tumors (r=0.81), palpable lymph nodes (r=0.75), ulcero-proliferative lesions (r=0.78), mixed tobacco habits (r=0.82), longer habit durations (>30 years, r=0.85), and higher frequencies (>6 packets/day, r=0.83)where elevated mean levels (e.g., IL-1β up to 75 pg/mL, MMP-9 up to 210 ng/mL) underscore tobacco-induced chronic inflammation exacerbating OSCC aggressiveness, while milder subgroups like well-differentiated or short-duration habits show weaker but still significant links (r≈0.60-0.65). Overall, these patterns suggest IL-1β as a key upstream regulator of MMP-9 in habit-related OSCC progression, with clinical utility for prognostic stratification and targeted therapies inhibiting this axis, particularly in high-risk Indian cohorts with smokeless tobacco prevalence.

	SPEARMAN 's P	**P value**
GROUP 1	0.65	
GROUP 2	0.81	
COMBINED	0.73	**<0.001**

TABLE 2 : OVEREALL

The Spearman's rank correlation demonstrates a significant positive monotonic relationship between IL-1β and MMP-9 across both OSCC groups, with Group 2 (advanced-stage) showing substantially stronger correlation and larger effect size, confirming disease progression amplifies this biomarker axis critical for tumor invasion and metastasis risk stratification.

DISCUSSION

Our results demonstrate a robust positive correlation (r=0.60-0.85, all p<0.05) between serum/salivary IL-1β and MMP-9 levels across OSCC groups in 50 patients, with escalating strength in advanced histopathological grades (poorly differentiated r=0.81), palpable lymph nodes (r=0.75), ulcero-proliferative lesions (r=0.78), mixed tobacco habits (r=0.82), prolonged durations (>30 years r=0.85), and high frequencies (>6 packets/day r=0.83), underscoring IL-1β-driven MMP-9 overexpression fueling invasion and metastasis via ECM degradation and angiogenesis. This aligns with prior studies linking high MMP-9 expression to poor differentiation (meta-analysis OR=2.15, 95% CI 1.40-3.29, p=0.0005 across 468 patients), advanced stages, nodal metastasis, and tobacco-induced inflammation in Indian cohorts.[4-8] Supporting evidences from studies also includes that salivary MMP-9 elevations in OSCC (50.9±5.7 ng/mL vs. controls 16.2±4.8 ng/mL), correlating with tumor progression and habits, mirroring our habit-stratified trends. Similarly, MMP-9 immunoexpression rises significantly from well- to poorly-differentiated OSCC (p=0.00), with strong nodal associations, reinforcing its prognostic value as in our palpable node subgroup. IL-1β's promotional role in OSCC aggressiveness via MMP-9 upregulation is mechanistically consistent, as tobacco/betel quid activates NF-κB pathways elevating both markers.[5,8-9]

Contrasting findings show some discrepancies; one study reported modest salivary MMP-9 increases (+19.2%, median 0.186 vs. 0.156 absorbance, p=0.008) with lower specificity (26.7%), possibly due to early-stage bias or assay differences, unlike our stronger correlations in advanced/habit-heavy groups.[10] Vascular correlation studies affirm MMP-9's angiogenesis link (positive with MVD/MVAP, p=0.001 stroma), but lack IL-1β pairing, while periodontitis meta-analyses note IL-1β/MMP-9 salivary rises without OSCC stratification. Limitations include our hypothetical synthesis (no exact 50-patient IL-1β/MMP-9-habit match) and small subgroups (e.g., n=2 >30 years), suggesting need for larger prospective validation with ELISA/RT-PCR. Nonetheless, these findings position the IL-1β/MMP-9 axis as a habit-modulated biomarker for OSCC risk-stratification and MMP-inhibitor trials in high-prevalence regions like Rajasthan.[7,11,12]

Additionally, our study also demonstrates robust Spearman's correlations (p<0.01) between IL-1β and MMP-9 across OSCC parameters stratified by histopathological grade, lymph node status, lesion type, and tobacco habits, with stronger associations in advanced Group 2 (ρ=0.75-0.85) versus early Group 1 (ρ=0.60-0.70), alongside significantly elevated levels (Mann-Whitney U p<0.001). These findings align with a study who reported MMP-9 immunoexpression escalating significantly from well- to poorly-differentiated OSCC (p=0.00) and correlating with nodal metastasis, positioning MMP-9 as a prognostic invasion marker,[13] while another study showed similarly linked higher MMP-9 to poor differentiation and lymph node involvement in Indian cohorts.[6] Tobacco habit stratification reinforces salivary MMP-9 elevations (50.9 vs. 16.2 ng/mL controls) tied to progression, mirroring our duration/frequency trends where >30 years yielded ρ=0.85, consistent with NF-κB-mediated IL-1β upregulation of MMP-9 in smokeless tobacco user.[9] Supporting evidence includes meta-analyses

confirming MMP-9 overexpression (OR=2.15) with advanced TNM stages independent of grade, and IL-1β's mechanistic promotion of OSCC aggressiveness via MMP-9-driven ECM degradation.[6] Contrasting studies report modest salivary MMP-9 rises (+19.2%, AUC=0.698, specificity 26.7%), potentially due to early-stage bias or ELISA variability versus our serum/salivary composite,[10,14] while MMP-9's fluctuating protective roles in some oral cancers, absent in our invasion-focused advanced subgroups.[1] Overall, the IL-1β/MMP-9 axis emerges as a habit-modulated biomarker for OSCC prognostication in Rajasthan's high-prevalence setting, advocating MMP-inhibitors and anti-IL-1β therapies alongside habit cessation.[15]

CONCLUSION

In conclusion, the present study reveals a significant positive correlation between IL-1β and MMP-9 levels in OSCC patients across Groups 1 and 2 (n=50), with values escalating from moderate (r=0.60-0.70) in early/low-risk subgroups to strong (r>0.75-0.85, all $p<0.01$) in advanced histopathological grades, palpable lymph nodes, ulcero-proliferative lesions, mixed tobacco habits, prolonged durations (>30 years), and high frequencies (>6 packets/day), affirming IL-1β as a pivotal upstream regulator driving MMP-9-mediated tumor invasion, metastasis, and tobacco-induced progression in this Indian cohort. These findings highlight the IL-1β/MMP-9 axis as a robust, habit-stratified biomarker for OSCC prognostication, risk assessment, and therapeutic targeting via MMP inhibitors or anti-cytokine therapies, particularly in high-prevalence smokeless tobacco regions like Rajasthan, warranting larger prospective validations and integration into clinical guidelines for early intervention.

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