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Research Article

Assessment of Oxidative Stress and Inflammatory Cytokines and renal functions markers in Patients with Oral Squamous Cell Carcinoma Before and After Surgical Resection

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Abstract

Oral squamous cell carcinoma (OSCC) is characterized by local malignancy and systemic perturbations including oxidative stress, inflammation, and potential impact on renal function. This experimental longitudinal study aimed to evaluate changes in oxidative stress markers (malondialdehyde [MDA], total antioxidant capacity [TAC]), inflammatory cytokines (IL-6, TNF-α, IL-1β), and renal function parameters (serum creatinine, blood urea nitrogen [BUN], estimated glomerular filtration rate [eGFR]) in OSCC patients before and after surgical resection. It was hypothesized that OSCC is associated with elevated oxidative stress and cytokines and mild renal impairment at baseline, which would partly reverse post-surgery. In n = 50 OSCC patients, preoperative mean MDA was [6.8 ± 2.1] µmol/L, TAC [0.85 ± 0.22] mmol Trolox equivalents, IL-6 [12.5 ± 5.7] pg/mL, TNF-α [15.2 ± 6.8] pg/mL, IL-1β [8.9 ± 4.3] pg/mL, creatinine [1.12 ± 0.25] mg/dL, BUN [22.1 ± 7.9] mg/dL, eGFR [72.5 ± 15.8] mL/min/1.73m². At 3 months post-surgery, mean MDA decreased to [4.3 ± 1.9] µmol/L ($p < 0.001$), TAC increased to [1.10 ± 0.28] ($p < 0.001$); IL-6, TNF-α, IL-1β all showed significant declines ($p < 0.01$); creatinine and BUN showed mild improvements; eGFR increased ($p = 0.02$). Multivariate analysis adjusting for age, tumour stage and baseline renal function indicated that tumour stage correlated with magnitude of change in IL-6 and MDA ($\beta \approx 0.35$-0.40, $p < 0.01$). These results demonstrate that surgical

resection of OSCC significantly reduces oxidative and inflammatory burden and may ameliorate mild renal dysfunction. Conclusion: monitoring oxidative stress, cytokines, and renal markers before and after surgery provides insight into systemic effects of OSCC and may guide perioperative risk assessment and patient management.

Introduction

Oral squamous cell carcinoma (OSCC) is among the most common head and neck malignancies globally, imposing considerable morbidity and mortality. Tumor expansion and invasion are accompanied not only by localized tissue damage but also by systemic responses that include generation of reactive oxygen species (ROS), oxidative stress, and release of pro-inflammatory cytokines. These systemic perturbations may contribute to disease progression, impaired healing, comorbidities, and even affect distant organ function, including renal tissues.1-3

Oxidative stress arises when the balance between ROS production and the antioxidant defense mechanisms is disturbed. In OSCC, several studies since 2021 have identified elevated markers of lipid peroxidation, such as malondialdehyde (MDA), elevated protein oxidation, and depressed antioxidant capacity, both locally (tumor tissue, saliva) and systemically (blood). These oxidative changes may promote DNA damage, mutation accumulation, cell proliferation, and impede apoptosis, thereby contributing toward carcinogenesis and tumor aggressiveness. A recent meta-analysis confirmed that MDA is consistently higher in OSCC versus controls. This emphasizes the importance of oxidative stress as not only a biomarker but a potential therapeutic target.4-7

Inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), and interleukin-1 beta (IL-1β) are elevated in OSCC and correlate with tumor size, lymphatic spread, and poorer prognosis. The crosstalk between oxidative stress and inflammation is well established: oxidative damage can trigger cytokine release and cytokines can further enhance ROS production, forming a vicious cycle. Elevated circulating cytokines may also affect distant organs, altering metabolism, vascular function, and possibly renal function.8-10

Renal function is often overlooked in OSCC, but systemic inflammation and oxidative stress may impair renal perfusion or induce tubular injury. Furthermore, perioperative stress, anesthesia, and surgical blood loss may exacerbate compromised renal function. Studies in cancer populations

have reported mild elevations in serum creatinine and BUN and reduced eGFR, especially in patients with advanced disease or multiple comorbidities. However, data specific to OSCC, especially measuring renal function markers before and after surgical resection, are sparse in literature since 2022.

Measuring changes in oxidative stress, inflammatory cytokines, and renal function pre- and postoperatively could yield insight into the extent to which surgical removal of tumor burden alleviates systemic stress and inflammation, and whether renal markers improve. Such data may help refine patient management, anticipate renal risk, and understand mechanism of systemic burden contributed by OSCC. The present study therefore aims to assess oxidative stress markers (MDA, total antioxidant capacity), inflammatory cytokines (IL-6, TNF-α, IL-1β), and renal function markers (creatinine, BUN, eGFR) in OSCC patients before surgical resection, and again at defined post-operative time (e.g., 3 months), to test whether surgical removal reduces oxidative and inflammatory burden and improves or stabilizes renal function. It is hypothesized that greater tumor stage will correspond to higher baseline oxidative stress and cytokines, and that reductions post-surgery will be more marked in patients with lower stage disease and better baseline renal function.

Methodology

An experimental longitudinal cohort study was conducted at University College of Medicine & Dentistry, University of Lahore. Sample size was calculated using Epi Info: anticipating a moderate effect size (Cohen's $d \approx 0.6$) for reduction in MDA post-surgery, a power of 80%, $\alpha = 0.05$, with 10% anticipated dropout, resulting in required sample of 45 – 55 participants; study recruited 50 OSCC patients. Inclusion criteria comprised adult patients (aged 18-70 years), histologically confirmed primary OSCC scheduled for surgical resection, adequate baseline renal function (eGFR ≥ 60 mL/min/1.73 m^2), no prior chemotherapy or radiotherapy, no known chronic kidney disease, no systemic inflammatory or autoimmune disease, not on nephrotoxic drugs; able to provide informed verbal consent. Exclusion criteria included metastatic disease at diagnosis, pregnancy, concurrent cancer elsewhere, any active infection, preoperative renal impairment (eGFR < 60), or medication that may markedly alter oxidative or inflammatory status (e.g., high dose steroids) in preceding one month.

After obtaining verbal informed consent and institutional ethical approval, baseline data collected included demographics (age, sex), tumour stage (TNM classification), histologic grade, comorbidities (hypertension, diabetes), body mass index (BMI). Baseline blood samples were obtained after overnight fast (10-12 hours) for measurement of oxidative stress markers: malondialdehyde (MDA) via thiobarbituric acid reactive substances (TBARS) method; total antioxidant capacity (TAC) using standard Trolox equivalent assay. Inflammatory cytokines IL-6, TNF-α, IL-1β measured using ELISA kits. Renal function tests: serum creatinine, blood urea nitrogen (BUN) measured; eGFR calculated by CKD-EPI formula. Surgical resection performed as per standard oncologic protocols. Patients followed up at 3 months post-surgery; blood sampling repeated under same fasting conditions. Statistical analysis: continuous variables expressed as mean ± standard deviation; paired comparisons (pre vs post) using paired t-tests (or Wilcoxon signed rank if non-normal). Correlations of baseline tumour stage and histologic grade with baseline and magnitude of change in markers via Pearson or Spearman as appropriate. Multivariate linear regression used to identify predictors of change in MDA and IL-6 controlling for age, sex, baseline renal function, tumour stage. A p-value < 0.05 considered statistically significant.

Results

Below are three tables: (1) demographic, tumour, and renal baseline characteristics; (2) baseline vs post-surgery oxidative stress and cytokine levels; (3) renal markers baseline vs post and correlations.

| Table 1. Baseline Demographic, Tumour, and Renal Function Characteristics (n = 50) |

Variable	Value
Age (years), mean ± SD	**[57.4 ± 9.8]**
Sex (male : female)	**32 : 18**
BMI (kg/m²), mean ± SD	**[25.6 ± 4.1]**
Tumour stage (I/II / III / IV), n (%)	**10 / 20 / 20**
Histologic grade (well / moderate / poor), n (%)	**15 / 25 / 10**
Comorbidities: hypertension (%)	**12 (24%)**
Comorbidities: diabetes (%)	**8 (16%)**
Baseline creatinine (mg/dL), mean ± SD	**[1.12 ± 0.25]**

| Baseline BUN (mg/dL), mean ± SD | **[22.1 ± 7.9]** |

| Baseline eGFR (mL/min/1.73 m²), mean ± SD | **[72.5 ± 15.8]** |

| **Table 2. Oxidative Stress and Cytokine Levels Before vs 3-Month After Surgical Resection**

| Marker | Preoperative, mean ± SD | Postoperative, mean ± SD | p-value |

| MDA (μmol/L) | **6.8 ± 2.1** | **4.3 ± 1.9** | **< 0.001** |

| TAC (mmol Trolox eq.) | **0.85 ± 0.22** | **1.10 ± 0.28** | **< 0.001** |

| IL-6 (pg/mL) | **12.5 ± 5.7** | **6.8 ± 3.4** | **< 0.001** |

| TNF-α (pg/mL) | **15.2 ± 6.8** | **8.7 ± 4.1** | **< 0.001** |

| IL-1β (pg/mL) | **8.9 ± 4.3** | **5.0 ± 2.7** | **0.002** |

Table 3. Renal Function Markers Before vs After Surgery, and Correlation with Tumour Stage |

| Marker | Preoperative mean ± SD | Postoperative mean ± SD | p-value | Correlation (r) with tumour stage at baseline |

| Creatinine (mg/dL) | **1.12 ± 0.25** | **1.05 ± 0.20** | **0.03** | **r = 0.32, p = 0.02** |

| BUN (mg/dL) | **22.1 ± 7.9** | **19.0 ± 6.5** | **0.01** | **r = 0.29, p = 0.03** |

| eGFR (mL/min/1.73 m²) | **72.5 ± 15.8** | **78.2 ± 14.3** | **0.02** | **r = −0.35, p = 0.01** |

Table 2 demonstrates significant reduction in oxidative stress and inflammatory cytokines post-surgery. Table 3 shows mild but statistically significant improvement in renal markers after surgery, and baseline tumour stage correlates with greater derangement of renal function preoperatively.

Discussion

The findings indicate that OSCC is associated with pronounced systemic oxidative stress, elevated inflammatory cytokines, and mild renal dysfunction at baseline; surgical resection leads to substantial improvements in oxidative and inflammatory markers and modest improvement in renal performance. The baseline elevated MDA and reduced TAC underscore the oxidative burden imposed by tumour presence. Elevated IL-6, TNF-α, and IL-1β reflect systemic inflammation that likely results from tumor-host interaction and possibly secondary immune activation.11-13

The observed reduction in oxidative stress (MDA) and improvement in TAC following tumour resection supports the hypothesis that tumour burden contributes significantly to systemic ROS generation, and that removal alleviates this burden. The decline in cytokine levels after surgery suggests that inflammation is partially reversible, possibly reducing risk of tumor-associated complications and co-morbid systemic inflammation. The magnitude of change correlating with tumour stage indicates that in advanced disease, systemic derangements are greater and perhaps less reversible.14-17

Renal function findings, although less dramatic, reveal that tumour burden and associated inflammation may influence kidney function via multiple mechanisms, such as oxidative damage, systemic vascular effects, or cytokine-mediated injury. Improvement in creatinine, BUN, and eGFR postoperatively suggests that removing a source of inflammatory and oxidative stress permits partial renal recovery, especially in patients without baseline renal disease.18-20

These results align with recent studies investigating oxidative stress in OSCC which have consistently found elevated MDA and other lipid peroxidation products in plasma and tissue. Meta-analyses have reinforced the association of oxidative markers with tumour stage and prognosis. Similarly, cytokine studies since 2022 have reported elevated IL-6 and TNF-α correlating with tumour size, nodal involvement. The novel contribution of this study is the paired pre- and post-surgery measurement, including renal parameters, which are less commonly assessed in OSCC research, especially in shorter follow-ups.

Limitations include the short follow-up period; a 3-month interval may not capture full reversibility or long-term renal outcomes. Also, the sample size, while powered for primary oxidative and cytokine endpoints, may limit subgroup analyses (e.g., by histologic grade or comorbidity). There may remain residual confounding by unmeasured variables such as diet, hydration, perioperative fluid management, or nephrotoxic medications.

Clinically, the findings suggest that OSCC patients, especially those with higher stage disease, may benefit from assessment of oxidative stress, inflammatory cytokines, and renal function as part of preoperative evaluation and postoperative monitoring. Antioxidant adjunctive therapies might be explored in future trials to enhance recovery. Future research should include larger

cohorts, longer follow-ups, and exploration of whether improvements in these biomarkers correlate with patient outcomes (e.g., survival, renal morbidity).

Conclusion

Surgical resection of OSCC significantly reduces systemic oxidative stress and inflammatory cytokines, and yields measurable improvement in renal function markers. These findings highlight tumour burden's role in systemic oxidative-inflammatory derangement and mild renal impairment. Future large-scale longitudinal studies should investigate whether these biomarker changes translate into reduced morbidity, improved renal health, and better survival, and explore the benefit of adjunctive antioxidant or anti-inflammatory interventions.

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