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Evaluation of Salivary Antioxidant Levels in Patients with Oral Squamous Cell Carcinoma

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Abstract

Salivary biomarkers have emerged as non-invasive tools for assessing oxidative stress, a pivotal factor in the pathogenesis of oral squamous cell carcinoma (OSCC). This study evaluates salivary antioxidant levels in OSCC patients compared to healthy controls to elucidate their diagnostic and prognostic utility. A case-control design was employed, enrolling 60 participants: 30 confirmed OSCC cases and 30 age- and gender-matched controls. Salivary samples were analyzed for total antioxidant capacity (TAC), superoxide dismutase (SOD), and glutathione peroxidase (GPx) using standardized assays. Results revealed significantly reduced TAC and enzymatic antioxidant levels in OSCC patients ($p < 0.01$). These findings suggest heightened oxidative stress in OSCC. Statistical analysis demonstrated a strong inverse correlation between antioxidant levels and disease severity ($p < 0.05$). This novel exploration emphasizes the role of oxidative stress markers in OSCC and their potential as diagnostic adjuncts. Further, these markers may provide insight into disease progression, underscoring the necessity for larger cohort studies to confirm their utility in clinical practice.

Keywords: Oral squamous cell carcinoma, salivary antioxidants, oxidative stress biomarkers.

Introduction: Oral squamous cell carcinoma (OSCC), the predominant malignancy affecting the oral cavity, represents a significant global health burden with a rising incidence and mortality rate, particularly in developing regions. Its multifactorial etiology involves a complex interplay between environmental, genetic, and lifestyle factors, such as tobacco use, alcohol consumption, and human papillomavirus infection. Despite advances in diagnostic and therapeutic strategies, the prognosis for OSCC remains suboptimal, with a five-year survival rate below 50% (Mishra et al., 2022). Early detection is critical for improving outcomes, necessitating the identification of reliable and non-invasive biomarkers.

Oxidative stress, defined as an imbalance between reactive oxygen species (ROS) and the antioxidant defense system, has garnered attention as a central mechanism in OSCC pathogenesis. Persistent oxidative stress induces genomic instability, promotes malignant transformation, and accelerates tumor progression (Kumar et al., 2023). Saliva, as a readily accessible biofluid, offers a unique medium for exploring oxidative stress markers due to its close proximity to the tumor microenvironment and its ease of collection. The assessment of salivary antioxidants has been proposed as a promising diagnostic adjunct for OSCC, potentially enabling early detection and risk stratification (Patel et al., 2021).

Existing research highlights reduced levels of enzymatic and non-enzymatic antioxidants in OSCC patients, reflecting an overwhelmed antioxidant defense system. However, studies investigating the correlation between antioxidant depletion and disease severity remain limited (Sharma et al., 2023). Furthermore, the application of advanced analytical techniques has facilitated the quantification of salivary biomarkers with improved precision, paving the way for their integration into routine clinical practice.

The present study aims to evaluate salivary antioxidant levels, including total antioxidant capacity (TAC), superoxide dismutase (SOD), and glutathione peroxidase (GPx), in OSCC patients and healthy controls. By establishing the association between oxidative stress biomarkers and disease severity, this investigation seeks to expand the current understanding of OSCC pathophysiology and underscore the clinical relevance of salivary diagnostics.

Additionally, this study addresses gaps in the literature by employing a robust statistical approach to analyze the diagnostic performance of these biomarkers. The findings are expected to provide new insights into the utility of salivary antioxidants as non-invasive tools for OSCC management, aligning with recent advances in precision oncology (Li et al., 2022).

This research builds on the premise that salivary biomarkers, as surrogates for systemic oxidative stress, hold immense potential for improving OSCC outcomes. By exploring their diagnostic and prognostic implications, this study contributes to the growing body of evidence supporting saliva as a "liquid biopsy" for oral cancers.

Methodology: This case-control study was conducted at University of Health Sciences, Lahore tertiary care center between January 2023 and July 2024. The study population included 60 participants, divided into two groups: 30 OSCC patients confirmed via histopathological examination and 30 age- and gender-matched healthy controls. The sample size was calculated using Epi Info software (version 7.2), with an expected effect size of 0.8, a power of 80%, and a significance level of 0.05. Participants provided verbal consent after receiving a detailed explanation of the study objectives.

Inclusion criteria encompassed newly diagnosed OSCC patients aged 18–65 years without prior treatment, while exclusion criteria included individuals with systemic diseases, concurrent malignancies, or antioxidant supplementation. Salivary samples were collected in the morning to minimize diurnal variations, ensuring participants refrained from eating, drinking, or smoking for at least two hours prior. Samples were centrifuged, and supernatants were stored at -80°C . TAC, SOD, and GPx levels were measured using commercially available kits. Statistical analyses, including independent t-tests and Pearson correlation, were performed using SPSS software (version 28.0). A p-value <0.05 was considered statistically significant.

Results

Table 1: Demographic Characteristics

Characteristic	OSCC Group (n=30)	Control Group (n=30)	p-value
Age (years)	55.2 ± 8.3	53.9 ± 7.8	0.48
Gender (M/F)	18/12	17/13	0.81

Table 2: Salivary Antioxidant Levels

Biomarker	OSCC Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
TAC (mmol/L)	0.92 ± 0.15	1.48 ± 0.20	<0.01
SOD (U/mL)	0.86 ± 0.12	1.35 ± 0.14	<0.01
GPx (nmol/min)	2.34 ± 0.27	3.12 ± 0.30	<0.01

Table 3: Correlation Between Biomarkers and Disease Severity

Biomarker	Correlation Coefficient (r)	p-value
TAC	-0.52	<0.05
SOD	-0.48	<0.05
GPx	-0.61	<0.05

Statistical analyses revealed significant reductions in antioxidant levels in OSCC patients. Correlations suggest oxidative stress markers are inversely associated with disease severity.

Discussion: Oxidative stress plays a pivotal role in the initiation and progression of various malignancies, including oral squamous cell carcinoma (OSCC). It results from an imbalance between reactive oxygen species (ROS) production and the antioxidant defense system. Elevated ROS levels can induce DNA mutations, promote angiogenesis, and inhibit apoptosis, all of which contribute to carcinogenesis (Zhang et al., 2021). This study highlights a marked reduction in salivary antioxidant levels, such as total antioxidant capacity (TAC), superoxide dismutase (SOD), and glutathione peroxidase (GPx), among OSCC patients compared to healthy controls. These findings align with the growing body of literature emphasizing the critical role of oxidative stress in oral carcinogenesis (Chen et al., 2022).

The depletion of TAC in OSCC patients indicates an overwhelmed non-enzymatic antioxidant system, which fails to neutralize the excessive ROS burden. TAC serves as a cumulative measure of all antioxidants, both enzymatic and non-enzymatic, and its significant reduction underscores systemic oxidative stress (Singh et al., 2023). Similarly, the decline in enzymatic antioxidants such as SOD and GPx suggests impaired scavenging of superoxide radicals and hydrogen peroxide, respectively. This disruption amplifies cellular oxidative damage, facilitating tumor progression (Patel et al., 2023).

Recent advancements in salivary diagnostics have opened new avenues for non-invasive biomarker discovery. Unlike serum or tissue biopsies, saliva offers ease of collection, cost-effectiveness, and minimal discomfort for patients. Moreover, its proximity to oral lesions enhances the relevance of salivary biomarkers in detecting OSCC (Kumar et al., 2023). The significant differences in antioxidant levels observed in this study support their utility in differentiating OSCC patients from healthy individuals. Furthermore, the strong inverse correlation between these markers and disease severity underscores their potential prognostic value.

Incorporating salivary antioxidants into routine screening programs could revolutionize OSCC diagnostics, particularly in resource-limited settings. Early detection is critical for improving survival rates, as it enables timely intervention and minimizes disease-related morbidity (Sharma et al., 2023). However, several challenges need to be addressed before implementing these biomarkers in clinical practice. Variability in salivary flow rates, dietary influences, and circadian rhythms may affect biomarker levels, necessitating standardized protocols for sample collection and analysis (Li et al., 2022).

This study contributes to the literature by providing statistically significant evidence of reduced antioxidant levels in OSCC patients. Previous studies have primarily focused on individual markers, but the comprehensive evaluation of TAC, SOD, and GPx provides a holistic view of the antioxidant defense system in OSCC (Zhao et al., 2022). The findings align with emerging research advocating for oxidative stress as a therapeutic target in oral cancer. Antioxidant supplementation or therapies aimed at restoring redox balance may hold promise as adjuvant strategies to conventional treatments (Fernandez et al., 2023).

The limitations of this study include its relatively small sample size and cross-sectional design, which precludes causal inferences. Longitudinal studies are warranted to explore temporal changes in antioxidant levels and their association with disease progression. Additionally, incorporating other oxidative stress markers, such as malondialdehyde or 8-hydroxydeoxyguanosine, could provide a more comprehensive understanding of the redox dynamics in OSCC (Ahmed et al., 2023).

Future research should focus on validating these findings in larger, multi-center cohorts and exploring the integration of salivary antioxidants with molecular biomarkers for enhanced diagnostic accuracy. The advent of omics technologies, such as metabolomics and proteomics, could further refine the identification of salivary biomarkers, paving the way for personalized OSCC management (Rodriguez et al., 2024). By bridging the gap between bench and bedside, such endeavors have the potential to improve patient outcomes and reduce the global burden of OSCC.

Conclusion

This study highlights the significant depletion of salivary antioxidants in OSCC patients, emphasizing their potential as diagnostic and prognostic markers. By addressing the gaps in understanding oxidative stress in OSCC, this research advocates for the incorporation of salivary biomarkers into clinical practice. Future studies should validate these findings in larger cohorts to facilitate their translational application.

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