

# Original Article

## Oxidative Stress a Link to Periodontal Disease and Oral Cancer

\*Shankarram V, \*\*Joysonmoses, \*\*Lakshmi Narayanan, \*\*Tamil Selvan

Reader \*, Professor\*\*, Department of Pedodontics, Thai Moogambigai Dental College, Chennai, India.



Dr. Shankarram Is an Upcoming Periodontist In Chennai Having Graduated From Ragas Dental College, He Completed His Postgraduation From Meenakshi Ammal Dental College In 2006. He Has Currently Enrolled for His Ph.D. Programme In Dr.M.G.R. Research Institute and University, Chennai, Tamil Nadu. He Is Working as a Reader in The Thaimoogambigai Dental College.

Corresponding author - **Shankarram V** ([mmhvhospital@gmail.com](mailto:mmhvhospital@gmail.com))

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### Abstract

The oral cavity is an entry of other systems of the body; it should not be viewed as an isolated area. Diseases that it lays down can have systemic impact and significantly affect the quality of life of individuals who suffer them. Periodontal disease is one of the oral health problems that most often affect the global population, lack of treatment leads to loss of tooth organs and consequently alters the digestion and nutrition, without considering other relevant aspects as phonation, aesthetics and social or emotional impact. The importance of periodontal disease has raised possible bidirectional relationships with systemic diseases such as diabetes, metabolic syndrome and cardiovascular disease. We address herein the role of oxidative stress in the pathogenicity of periodontal disease. In the same context, another disease that has become relevant in our days is the oral cancer. Detection of the reactive oxygen species in the periodontitis patients and oral cancer patients reveal the relationship between the oxidative stress in periodontitis and oral cancer patients.

**Key Words:** Oxidative stress, Periodontal disease, Oral cancer

### Introduction

Oxidative stress is the systemic disturbance caused by the increased Reactive oxygen species a biological system's ability to readily detoxify the reactive intermediates or to repair the resulting damage. Disturbances in the normal redox state of cells can cause toxic effects through the production of peroxides and free radicals that damage all components of the cell, including proteins, lipids, and DNA. Oxidative stress from oxidative metabolism causes base damage, as well as strand breaks in DNA. Base damage is mostly indirect and caused by reactive oxygen species (ROS) generated, e.g. O<sub>2</sub><sup>-</sup> (superoxide radical), OH (hydroxyl radical) and H<sub>2</sub>O<sub>2</sub> (hydrogen peroxide)<sup>1</sup>. In humans, oxidative stress is thought to be involved in the development of Asperger syndrome<sup>2</sup>, ADHD<sup>3</sup>, cancer<sup>4</sup>, Parkinson's disease<sup>5</sup>, Lafora disease<sup>6</sup>, Alzheimer's disease<sup>7,8</sup> atherosclerosis<sup>9</sup>, heart failure<sup>10</sup>, myocardial infarction<sup>11,12</sup>, fragile X syndrome<sup>13</sup>, Sickle Cell Disease<sup>14</sup>, lichen planus<sup>15</sup>, vitiligo<sup>16</sup>, autism<sup>17</sup>, infection<sup>18</sup>, chronic fatigue syndrome<sup>19</sup>. Periodontitis<sup>20</sup>. Epidemiological data show that the incidence of this neoplasm has been increasing in several countries. The impact of oral cancer on patients, who suffer it, is devastating. The role of oxidative stress in the development of this disease and some alternatives for its treatment, are topics addressed in this brief. Periodontitis and oral cancer are two oral diseases and a sample of the plethora of effects that oxidative stress may have at local and systemic level. So this study analyses the reactive oxygen species in saliva samples thereby proving their role in periodontitis and oral cancer.

### Objectives

The study has following objectives

1. To detect the oxidative stress in periodontitis

patients and oral cancer patients

2. To compare the oxidative stress between oral cancer patients and periodontitis

### Study groups

The case control study was done in department of periodontology under the ethical clearance from Dr. MGR UNIVERSITY And Research Institute three groups n=25 was selected

1. Group of periodontitis (n=25)
2. Group of oral cancer (n=25)
3. Group of healthy controls (n=25)

### Materials and methods

The saliva samples were collected from the three groups and stored in the plastic bottles, and the study done in regenix laboratory, Chennai. Oxidative stress status was assessed by measuring the total antioxidant capacity (TAOC) and biomarkers of oxidative stress 8-hydroxy-2-deoxyguanosine (8-OHdG) and malondialdehyde (MDA) in saliva and the activity of some of the main antioxidant enzymes glutathione peroxidase (GPx) and superoxide dismutase (SOD).

GPx and SOD activities and TAOC levels were determined using a competitive ELISA kit (Cayman Chemical Company; Item numbers 703102, 706002, and 709001, resp.) according to the manufacturer's instructions. MDA levels were measured with NWLSS Malondialdehyde Assay (Northwest Life Science Specialities; Catalog number NWK-MDA01) following the manufacturer's instructions. 8-hydroxy-2-deoxyguanosine (8-OHdG) levels were measured with NWLSS High Sensitivity 8-OHdG ELISA (Northwest Life Science Specialities; Catalog number NWK-MDA01) following manufacturer's instructions.

## Statistical Analysis

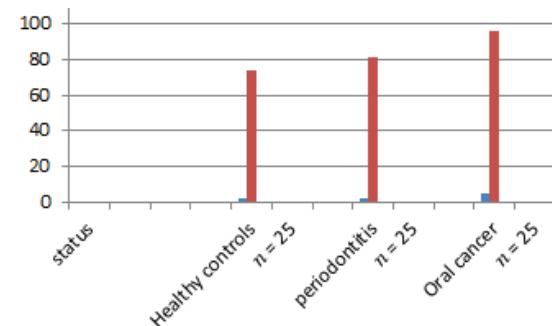
All results shown are expressed as mean and 95% confidence interval. Statistical comparisons between groups were assessed by Mann-Whitney or Kruskal-Wallis tests. The linear trend between groups was analyzed by the Jonckheere-Terpstra test. Multivariate linear regression predictive models were made with the different oxidative stress parameters as the dependent variable. The independent variables were age, gender, smoker (as confounding variables).

## Results

We obtained a highly significant elevation of all oxidative stress marker levels except for that of SOD. Periodontitis group and oral cancer denoted increased oxidative stress level. Therefore, the presence of oxidative stress in periodontitis and oral cancer is significant compared to healthy group.

status	Oxidative stress parameters				
	8-OHdG <sup>1,2</sup> (ng/ml)	GPx <sup>1,2</sup> (U/l)	TAOC <sup>1,2</sup> (mM)	SOD <sup>1,2</sup> (U/ml)	MDA <sup>1,2</sup> (nM)
Healthy controls	2.20 <i>n</i> = 25 (1.88–2.52)	75.04 (72.35–77.72)	0.91 (0.80–1.01)	3.24 (3.16–3.31)	4.43 (3.61–5.24)
periodontitis	2.33 <i>n</i> = 25 (1.84–2.82)	80.99 (76.89–85.15)	1.03 (0.89–1.17)	3.62 (3.37–3.86)	4.51 (3.95–5.68)
Oral cancer	5.54 <i>n</i> = 25 (4.96–6.12)	95.58 (93.12–98.04)	1.09 (1.01–1.17)	4.17 (3.91–4.42)	5.94 (5.04–6.84)

**Table 1:** Oxidative stress parameters and periodontal status



**Table 2:** Comparison between the three groups

## Discussion

The pathological events which lead to the destruction of the periodontium during inflammatory periodontal disease have been related to the effect of the imbalance between oxidants and antioxidants in patients with periodontal disease<sup>20</sup>.

ROS are generated predominantly by PMN during an inflammatory response<sup>21</sup>. It has been suggested that the bacterial species in subgingival plaques and the PMN response are important factors in the changes in periodontal disease status. An increase in ROS leads to the destruction of periodontal tissue, and it is one of the most important causes of periodontal disease. The present study has demonstrated significant changes in oxidative stress by measuring different oxidative stress

markers (8-OHdG, MDA, GPx, SOD, and TAOC) that increased with worsened periodontal status.

The involvement of free radicals in cancer development has been studied for 3 decades, and there is sufficient evidence that implicates theirs in the multistage theory of carcinogenesis. Free radicals are products of the oxidation-reduction systems of the cell and its participation in cellular metabolic functions is essential for cell survival. A classic example is the electron transport chain in mitochondria. However, in what pathological conditions, free radicals can become deleterious?

In fact, what are the results of its harmful effects. They are proposed to cause diverse DNA alterations like: punctual mutations, DNA base oxidations, strand breaks, mutation of tumor suppressor genes and can induce overexpression of proto-oncogenes<sup>22</sup>. Several works explore the levels of oxidative stress in patients with oral cancer<sup>23</sup> most of them quantified the products of lipid-peroxidation (mainly malonaldehyde) and contrast them with the activity of antioxidant enzymes or exogenous antioxidants levels in blood or even saliva. The results agree that there is an imbalance between the high amount of free radicals and insufficient antioxidant system activity. Added to this, some researchers have observed that high levels of lipid-peroxidation combined with low levels of thiols and antioxidant status, correlate with poor survival rate in patients with oral cancer<sup>24</sup>. It should be added that oxidative protein damage participates in facilitating the development of cancer. The present study has demonstrated significative changes in oxidative stress by measuring different oxidative stress markers (8-OHdG, MDA, GPx, SOD, and TAOC) that increased in oral cancer.

Our results agree partly with Canakci et al.<sup>25</sup>. In salivary samples from 30 patients with chronic periodontitis and 30 periodontally healthy controls, these authors obtained higher salivary 8-OHdG and MDA levels and lower salivary antioxidant activities that seem to reflect increased oxygen radical activity during periodontal inflammation.

## Conclusion

Certainly, the main limitation of the study has been the small sample size, but the study could confirm the possible linear correlation between markers of oxidative stress and the periodontitis and oral cancer. Further studies with larger sample size should continue this line of research. In conclusion, the determination of oxidative stress levels could be a potent tool in controlling the development of periodontitis and tool in detection of oral cancer.

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