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ORIGINAL ARTICLE

ASSOCIATION BETWEEN PERIODONTAL DISEASE AND HEAD AND NECK CANCER AND ESTIMATION OF C -REACTIVE PROTEIN: A CLINICAL AND BIOCHEMICAL STUDY

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ABSTRACT:

Background: Moderately elevated serum C-reactive protein (CRP) concentration is a systemic marker of inflammation and a documented risk factor for head and neck cancer. Unrecognized infections, such as periodontal disease, may induce an acute-phase response, elevating CRP levels. **Objectives:** The objective of this study was to associate the Periodontal status and serum C – reactive protein level with Head and neck cancer patients and systemically healthy chronic periodontitis patients. **Methods**: Thirty individuals; 15 diagnosed with head and neck cancer and 15 systemically healthy patients with chronic periodontitis were analyzed. The periodontal evaluation was done using clinical attachment level (CAL), probing depth (PD) and gingival index (GI). Serum CRP was quantified in milligrams per liter using an Immunostat C – Reactive protein kit. **Results:** There is a significant increase in the GI, PD CAL and CRP in the Head and neck cancer patients as compared to the chronic periodontitis cases ($P < 0.05$). Serum CRP concentration was positively correlated with mean GI ($P<0.001$), mean PD ($P<0.001$) and mean CAL ($P<0.001$). **Conclusion:** This study suggests a positive association between periodontal disease and serum CRP concentration in patients with head and neck cancer. However, more longitudinal studies are necessary to determine the exact causal relationship between serum CRP concentration and chronic periodontitis.

Keywords: C-reactive protein, Head and neck cancer, Periodontitis

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INTRODUCTION

Periodontitis is a local inflammatory process mediating the destruction of periodontal tissues, triggered by bacterial insult.[1] More recently, a link between periodontal disease and cancer has been suggested through several studies looking both at specific types of cancers and at the overall total cancer rate and the relationship to periodontal disease. The scientific rationale behind the proposed association is that inflammation is a major factor in both periodontal disease and cancer. Oral cancer, gingival squamous cell carcinoma in particular, has been known to mimic advanced periodontal disease in clinical appearance showing similar symptoms of swelling, bleeding, tooth mobility, deep periodontal pockets, and bone destruction.[2] Inflammation has been hypothesized to increase the risk of cancer.[3]

CRP was first reported by Tillett and Francis in 1930 and was named so because it was discovered as a substance in the serum of patients with acute inflammation that reacted with the C-(capsular) polysaccharide of *Pnuemococcus.*[4] It is normally present in ng/ml quantities but may increase dramatically to hundred of µg/ml within 72hrs following tissue injury.[5] It is regulated by cytokines like interleukin-6 (IL- 6), interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α).[6,7]

Since Periodontal infection is considered to be one of the risk factors for Head and neck cancer, an attempt was made in this study to associate the periodontal status and C – reactive protein level with Head and neck cancer patients and systemically healthy chronic periodontitis patients.

MATERIAL AND METHODS

Study Population

The study population comprised of thirty subjects out of which 15 were diagnosed with Head and neck cancer and the remaining 15 were recruited from the routine OPD at the Department Of Periodontics.

- Case group: 15 Head and neck cancer patients
- Control group: 15 systemically healthy; Chronic Periodontitis patients.

Inclusion Criteria:

1. Subjects with a minimum complement of 20 teeth.
2. Controls who are systemically healthy.
3. Periodontal health was defined as the absence of gingival pockets ≥4 mm and absence of attachment loss ≥3 mm with no BOP. Periodontal disease was defined as two or more tooth sites with PD ≥ 4 mm or CAL of 4 mm that bled on probing.

Exclusion Criteria

1. Subjects in the control group with any systemic disease
2. Patients who have undergone any periodontal treatment in the last 6 months.
3. Patients with recurrence of Head and Neck cancer.
4. Pregnant women or lactating women.
5. Subjects who are tobacco or alcohol users.

Screening Examination included recording of medical, dental history and whole mouth clinical periodontal measurements at six sites per tooth (mesio-buccal, mid-buccal, disto-buccal, disto-lingual, mid-lingual, mesio-lingial) for Probing depth and Clinical attachment level (CAL). Gingival index [Loe and Silness, 1963] was also recorded to measure the gingival status of every individual.

Oral Examination

During the oral examination, the following clinical data were recorded.

1.) Gingival index (GI) given by Loe and Silness in 1963
2.) Probing depth (PD)
3.) Clinical Attachment Level (CAL)

PD and CAL at six sites per tooth are measured for all teeth using a William's graduated periodontal probe.CAL was measured as the distance between the cemento-enamel junction and the base of the periodontal pocket. Both PD and CAL, rounded to the nearest 1mm, are measured at six sites (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual and disto - lingual).

Sample Collection and Preparation

Blood samples (10 ml) were collected from patients between 11:00 am and 12:00 am. Collected blood samples were then sent for investigation. Immunostat C – Reactive protein kit was used to estimate the C-reactive protein levels.

STATISTICAL ANALYSIS

The data obtained was statistically analyzed using Descriptive analysis (Mean, Standard deviation, Frequency, Percentage).To compare the clinical parameters and serum CRP between two groups , independent student's 't' test was used. Pearson's correlation was used to evaluate the association between the two groups. The level of significance for the study was 5%.

RESULTS

There is a significant increase in the GI, PD CAL and CRP in the Head and neck cancer patients as compared to the chronic periodontitis cases (P value <0.05) (Table I).

Table I: Independent student's 't' test for comparison of Gingival Index (GI), Probing Depth (PD), Clinical Attachment Level (CAL) and C – Reactive Protein (CRP) between case and control groups.

	Group	N	Mean	Std. Deviation	t	df	P Value
GI	Head and neck cancer patients	15	1.847143	0.534278	3.885	19.46	**0.001**
	Chronic periodontitis	15	1.224	0.282989			
PD	Head and neck cancer patients	15	5.764286	0.457497	8.165	27	**≤0.001**
	Chronic periodontitis	15	4.562667	0.328774			
CAL	Head and neck cancer patients	15	4.692143	0.606315	5.607	18.131	**≤0.001**
	Chronic periodontitis	15	3.695333	0.283092			
CRP	Head and neck cancer patients	15	5.425	4.348593	2.807	13.927	**0.014**
	Chronic periodontitis	15	2.104667	0.849831			

The mean GI, CAL, PD and CRP are significantly higher in the Head and neck cancer patients (Graph I). Serum CRP concentration was positively correlated with mean GI (P<0.001), mean PD(P<0.001) and mean CAL(P<0.001) (Table II).

Graph I: Comparison of mean Gingival Index (GI), Probing Depth (PD), Clinical Attachment Level (CAL) and C – Reactive Protein (CRP) between case and control groups.

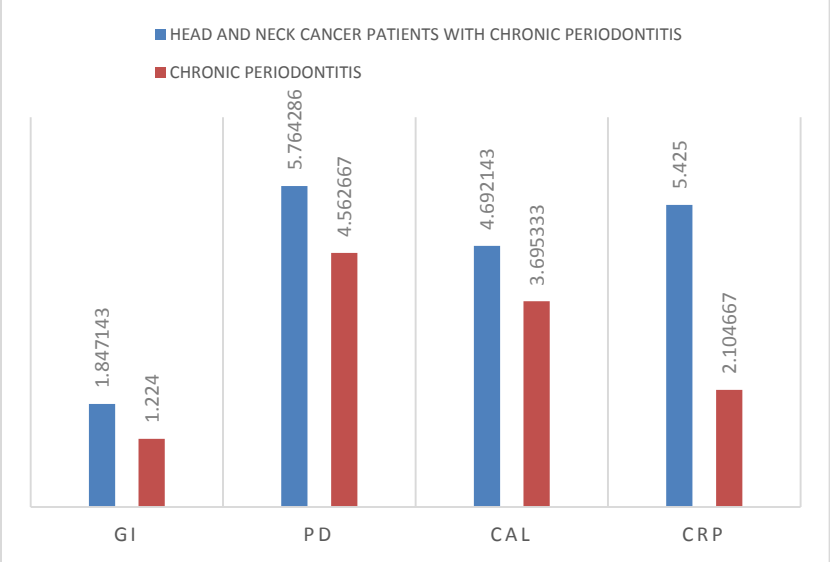

Table II: Pearson's Correlation test for comparison between GI, PD,CAL and CRP between case and control groups

GROUP			GI	PD	CAL
Chronic Periodontitis	GI	Pearson Correlation			
		Sig. (2-tailed)			
		N			
	PD	Pearson Correlation	.046		
		Sig. (2-tailed)	.871		
		N	15		
	CAL	Pearson Correlation	.433	.507	
		Sig. (2-tailed)	.107	.054	
		N	15	15	
	CRP	Pearson Correlation	.617*	.308	.890**
		Sig. (2-tailed)	**.014**	.265	**<0.001**
		N	15	15	15
Head And Neck Cancer Patients With Chronic Periodontitis	GI	Pearson Correlation			
		Sig. (2-tailed)			
		N			
	PD	Pearson Correlation	.968**		
		Sig. (2-tailed)	.000		
		N	14		
	CAL	Pearson Correlation	.936**	.956**	
		Sig. (2-tailed)	**<0.001**	**<0.001**	
		N	14	14	
	CRP	Pearson Correlation	.805**	.878**	.829**
		Sig. (2-tailed)	.001	**<0.001**	**<0.001**
		N	14	14	14
Combined	GI	Pearson Correlation			
		Sig. (2-tailed)			
		N			
	PD	Pearson Correlation	.807**		
		Sig. (2-tailed)	**<0.001**		
		N	29		
	CAL	Pearson Correlation	.892**	.922**	
		Sig. (2-tailed)	**<0.001**	**<0.001**	
		N	29	29	
	CRP	Pearson Correlation	.817**	.752**	.835**
		Sig. (2-tailed)	**<0.001**	**<0.001**	**<0.001**
		N	29	29	29

DISCUSSION

The results of this study demonstrated elevated concentrations of the acute-phase reactant serum CRP in individuals with head and neck cancer as compared to chronic periodontitis (Graph I). Thus, it seems that periodontal disease may serve as either a chronic or an acute stimulus of hepatic CRP. This might be explained by a reciprocal process in the liver. As part of the systemic inflammatory response to the tumor, interleukin-6 produced by the tumor stimulates liver production of acute phase reaction proteins, such as CRP.[8]Pearson's correlation test shows a significant association between serum CRP concentration and mean gingival index, probing depth and clinical attachment level (Table II).

Elevated serum CRP in periodontitis patients is associated with high levels of infection with periodontal pathogens.[9,10]Various studies[11-13] have proved a positive association between the presence of chronic periodontitis and high serum CRP levels because it is biologically plausible that inflammatory mediators (IL-1, IL-6 and TNF-α) are released under the conditions of periodontitis. These mediators of inflammation have the ability to stimulate the hepatocytes to produce CRP. Similarly, it can be expected that, in the presence of chronic periodontitis, higher serum CRP levels would be found. Pitiphat et al. also gave similar results for Porphyromonas gingivalis.[14] Dye et al.,[15] reported a high serum titre to P. gingivalis and the presence of periodontal disease which are independently related to high CRP levels. Our results support these findings indicating an association between serum CRP concentration and periodontal disease.

Patients with cancer of the oral cavity can be in poor nutritional condition. For esophageal cancer, a correlation has been shown between elevated serum CRP concentration and malnutrition with impaired immunity.[16] However, a study by Kruse et al did not support a correlation between preoperative CRP levels and development of recurrence or metastases.[17]

The present study has several limitations. Disease duration and nutrient intake could not be investigated which may have influenced serum CRP levels. These data might increase the reliability of the results about the relationship between serum CRP concentration and oral health status.

Hence, more longitudinal studies are necessary, as the cross-sectional design of this study does not allow for an assertion of causality between serum CRP and periodontitis.

CONCLUSION

A positive association between Head and Neck cancer and chronic periodontitis is seen in terms of the periodontal status. CRP increased markedly in Head and Neck Cancer patients than in systemically healthy patients with chronic periodontitis. However, there is insufficient evidence to recommend periodontal therapy to control high-normal values of CRP, and it has not been demonstrated that reducing CRP levels improves health. Instead, the findings from this study highlight the benefits of maintaining good periodontal health for a robust lifestyle.

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