International Journal of Health Sciences
March 2021, Vol. 9, No. 1, pp. 83-88
ISSN: 2372-5060 (Print), 2372-5079 (Online)

Published by American Research Institute for Policy Development
DOI: 10.15640/ijhs.v9n1a11
URL: https://doi.org/10.15640/ijhs.v9n1a11

Impact of Cigarette Smoking on Serum C-Reactive Protein Level among Sudanese Patients with Chronic Periodontitis at Khartoum Teaching Dental Hospital

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Abstract:

Background: The C-reactive protein is a non-specific inflammatory acute-phase plasma protein whose levels rise in response to inflammation. An association has been demonstrated between chronic periodontal disease and an elevated level of C-reactive protein. Smoking is an established risk factor for periodontal disease. Therefore, the combination of chronic periodontit is and smoking may be a high risk for individual health. **Methods:** An observational analytical cross-sectional hospital-based study was conducted on 84 participants (49 men and 35 women) categorised into four groups; Group A: included systematically healthy non-smokers without chronic periodontitis. Group B: included systematically healthy non-smokers with chronic periodontitis. Group C: included systematically healthy smokers without chronic periodontitis, while Group D: included systematically healthy smokers with chronic periodontitis. **Results:** The independent sample t-test demonstrated no statistically significant differences inthe serum levels of CRP between groups (A & B), (C & D), (A & C), (B & D) using a significant level (0.05). **Conclusions**: The present study concluded that (I) periodontal disease does not significantly affect the serum levels of C reactive protein (II) smoking does not contribute to an elevated level of C reactive protein (III) smoking has no impact on serum level of C reactive protein on periodontitis patients.

Keywords: Cardiovascular disease, chronic periodontitis, high sensitivity C-reactive protein, inflammatory burden, smoking

Text

1.Introduction:

Periodontal diseases are inflammatory conditions that affect the tissues around the teeth(1). Periodontal diseases are affected by many modifiable and non-modifiable risk factors that play a crucial role in an individual's response to periodontal infection. Identification of these risk factors facilitates targeting patients for prevention and treatment (2). One of the most common modifiable risk factors affecting the periodontium is smoking, which suggestively raises the risk for periodontitis and the severity of the illness (5).

Numerous cross-sectional studies have investigated chronic periodontitis as a possible risk factor for atherosclerosis and subsequent cardiovascular disease (7). In addition, the Khouja et al. study suggests that smoking plays an effect modifier in the relationship between periodontal and cardiovascular disease (3).

C-reactive protein (CRP), a pentameric plasma protein that participates in the systemic inflammatory response, is regulated by the cytokines, interleukin-1 (IL-1), interleukin-6 (IL- 6), and Tumour Necrosis Factor-Alpha (TNF-α) (14). C-reactive protein (CRP) levels have been associated with smoking, obesity, triglycerides, diabetes, and periodontal disease (14).

The present study throws light on the overall management outcome of the periodontal disease and also on the effect of smoking. The dentists and relevant medical staff need to critically investigate and be more precise in managing the patients with smoking and chronic periodontitis in Sudan.

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The outcome of this research can also help national health authorities in Sudan to adjust and promote their strategies and plans of action regarding the smoking-related health education issues in the context of periodontal health

The present study aims to study the impact of cigarette smoking on the serum level of C-reactive protein among Sudanese patients with chronic periodontitis at Khartoum dental teaching hospital. As C-reactive protein levels rise during inflammation, this study is helpful to measure the severity of periodontitis between smokers and non-smokers by using C-creative protein as a biomarker.

2. Participants and Methods:

An observational, analytical cross-sectional hospital-based study was conducted at the Khartoum Teaching Dental Hospital among 84 systemically healthy participants.A systematically simple random sampling method was applied to recruit the study participants.

The participants were not taking medications in the previous three months, non-pregnant or lactating women who have not undergone periodontal therapy during the last three months and non-cigarettes and shisha smokers or snuff dippers.

The participants were categorised into four equal groups, each consisting of 21 participants aged 18 years or more of both genders:

Group A: included systematically healthy non-smokers who have not smoked 100 or more cigarettes in their lifetime and were not diagnosed with chronic periodontitis.

Group B: systematically healthy, non-smokers diagnosed with chronic periodontitis (clinical attachment loss ≥ 1, periodontal pocket depth ≥ 4 in at least two non-adjacent teeth).

Group C: systematically healthy smokers, those who smoked 100 or more cigarettes on their lifetime, and those who were not diagnosed with chronic periodontitis.

Group D: included systematically healthy smokers with chronic periodontitis

Following the ethical approval from the Research Ethics Committee of the Educational Development Centre (RECEDC), Sudan Medical Specialization Board (SMSB), the Federal Ministry of Health (FMOH) and Khartoum Teaching Dental Hospital (KTDH). Following the explanation of the goals and procedure of the study and signing a written consent form in Arabic from the eligible participants, the data was collected. For illiterate participants, the form was read to them either by the investigator or a co-patient.

The periodontal parameters were assessed using the gingival index according to Löe and Silness (1963) (4), plaque index according to Silness and Löe (1964) (5), the probing pocket depth and the loss of clinical attachment loss according to Glavind and Löe (1967) (6) on all teeth present at six points (mesiobuccal, mid-buccal, distobuccal, distolingual, mid-lingual, and mesiolingual) with the aid of a dental mirror, and a graduated Williams periodontal probe. Partially erupted teeth, retained roots, teeth with a periapical lesion and third molars were excluded.

Chronic periodontitis was diagnosed according to the presence of a pathological periodontal pocket with probing pocket depth (PPD) more than or equal to 4 mm and a clinical attachment loss (CAL) of more than or equal 1 mm in at least two non-adjacent teeth (7).

A single qualified nurse drew venous blood sample using a blood vacuum tube for the biochemical tests from the participants. Before the needle was inserted, a tourniquet was applied around the participant's upper arm, and the puncture site was swapped with an antiseptic swap. Once 5 mLblood was collected into a vacuum tube, the tourniquet was released to restore circulation before the withdrawal of the needle. The puncture site was covered with a Band-Aid.

The blood sample was stored in a cold container and transported to the laboratory[3] for subsequent centrifugation and analysis by a single qualified laboratory technician. When the test could not be carried out on the same day, the serum was stored at 2-8 °C for up to 48 hours. The samples were frozen when analysis could not be conducted after 48 hours. The CRP levels were measured using a fully automated open system, a high-sensitivity C-reactive protein (hs-CRP) test. The CRP reagent kit was based on an immunological reaction between CRP antisera bound to biologically inert latex particles and CRP in the test specimen. Latex particles coated with an antibody specific to human CRP aggregate in the presence of CRP from the sample forming immune complexes.

The immune complexes cause an increase in light scattering, which was proportional to the concentration of CRP in the serum. The light scattering was measured by reading turbidity (absorbance) at 570 nm. The CRP concentration was determined from a calibration curve developed from CRP standards of known concentration.

[3] Rayan Specialised Laboratory, Khartoum, Sudan

2.1. Statistical analysis:

The data was collected, coded and locked in a password-protected computer at the principal investigator's office to ensure patient data confidentiality and privacy. Data entry and analyses of results were done using the Statistical Package for Social Sciences (SPSS)[4]. Ver. 23.0 for Windows software with the assistance of a professional biostatistician.

As the data were normally distributed, inferential statistics using the parametric independent sample t-test was performed for comparison between means of two groups. The level of significance was set at p-values < 0.05.

Descriptivestatisticssuchasmeanandstandarddeviation(SD)forcontinuousvariablesandfrequencyandpercentageforcategoricalvariableswere determined.

3. Results:

Eighty-four participants (49 women and 35 men), 42 non-smokers and 42 smokers with and without chronic periodontitis were grouped into four groups with 21 participants in each group. In group A, the mean age was 31.25 ±6.7 years while in group B the mean age was 35.35 ±11.9 years, in group C the mean age was 26.9 ±5.4 years,while in group D, it was 41.09 ±10.62 years (Table 1).

A higher percentage of male participants (57.1%) were seen in group A while in group B the percentage of females was (55%) while the males made up (45%). The males were higher in both groups C and D (61.9%), (66.7%), respectively(Table 2).

The study revealed that the mean duration of smoking in group C (smokers without chronic periodontitis) was 6.9± 5.94 years ranging between 4 months to 22 years, and the mean number of cigarettes smoked per day in the same group was 8.71 ±4.77 per day ranging between 2-15 cigarettes per day (Table 3 and Table 4).

While in group D (smokers with chronic periodontitis), the mean duration of smoking was 17.8 ±10.07 years ranging between one year to 36 years, and the mean number of cigarettes smoked per day was 12.42 ±6.66 per day ranging between 2-30 cigarettes per day (Table 3 and Table 4).

The Independent sample t-test indicated no significant overall differences of CRP serum levels between groups (A &B), (C&D), (A&C), (B&D), (A&D), (B&C) ($p \leq 0.05$) at 0.05 level of significance (Table 5).

Table 1: Age distribution of the groups' understudy

Group	Mean ± (SD) (Years)	Age range (years)
Group A: Non-Smoker &Healthy	31.25 ±6.7	21-43
Group B: Non-Smoker &Chronic periodontitis	35.35 ±11.9	20-66
Group C: Smoker &Healthy	26.90 ±5.4	20-38
Group D: Smoker & Chronic periodontitis	41.09 ±10.62	20-60

Table 2: Gender distribution of all study groups

Grouping	Group A (Non-Smoker &Healthy) N (%)	Group B (Non-Smoker &Chronic periodontitis) N (%)	Group C (Smoker &Healthy) N (%)	Group D (Smoker & Chronic periodontitis) N (%)
Male	12(57.1)	10 (45)	13(61.9)	14(66.7)
Female	9(42.9)	11 (55)	8(38.1)	7(33.3)

Table 3: Duration of Smoking

Group	Mean ± (SD.)	Range
Group C (Healthy& smokers)	6.9 ±5.94	4 months-22 years
Group D (CP& smokers)	17.8 ±10.07	1 year-36 years

[4]SPSS Software | IBM https://www.ibm.com › analytics › SPSS-statistics-software

Table 4: Number of cigarettes smoked per day

Group	Mean ±(SD.)	Range
Healthy	8.71 ±4.77	2 – 15
Chronic periodontitis	12.42 ±6.66	2 - 30

Table 5: Comparison between CRP serum levels in different groups

Groups		P-value
Group A	**Group B**	
7.09 ±3.54	6.54 ±3.54	<0.89
Group C	**Group D**	
7.02 ±3.47	8.47 ±3.08	<0.77
Group A	**Group C**	
7.09 ±3.54	7.02 ±3.47	<0.95
Group B	**Group D**	
6.54 ±3.54	8.47 ±3.08	<0.64
Group A	**Group D**	
7.09±3.54	8.47±3.08	<0.67
Group B	**Group C**	
6.54±3.54	7.02±3.47	<0.17

4. Discussion:

The current study has not shown that inflammatory periodontal disease contributed to elevated CRP serum levels despite using high sensitivity CRP assay and excluding any subject with any other infections or inflammatory conditions and pregnant and lactating women.

A possible explanation of the insignificant association between CP and CRP serum levels could be that a confounder such as the effects of obesity could be a critical determinant of CRP levels among adults and that adipose tissues have been considered a source of low-grade inflammation (8). Also, the present study did not assess confounders such as cholesterol level, eating protein-rich meals, sleep disorders, and depression. Therefore, these confounders may have influenced the study findings(9).

As the severity of periodontal disease increases, the relationship between CRP serum levels and periodontitis also increases. This association has been demonstrated in various studies and that the relationship between CRP serum levels and periodontal disease is typically found in older populations with more advanced disease; therefore, the presence of an association between CRP serum levels and periodontitis depends on the severity of the disease (10–12).

In the current study, the severity of periodontal disease was significantly less than anticipated because most of the study participants had moderate periodontitis, which may explain the lack of an association between periodontal disease and elevated CRP serum levels that may confound the establishment of a relationship between chronic periodontitis and elevated CRP serum levels.

The result of the present study was in line with the findings of Bretz*et al.*, who examined the levels of various systemic markers for inflammation, including CRP with periodontal diseases parameters of older people. Bretz*et al.* noticed that periodontal disease was not associated with high levels of serum CRP; however, cigarette smoking, diabetes mellitus, body mass index, gender and race were significantly associated with higher CRP serum levels (13). A study by Delange*et al.* among an Indian/Alaskan population in southern California also failed to illustrate a significant association between periodontal status and CRP levels (14).

However, a study conducted by Marcaccini*et al.* among middle-aged adults also found a significant difference in the levels of IL-6 between control participants and patients with periodontal disease; however, the study did not identify a significant difference in CRP levels (15).

Additionally, the present study's findings were similar to those of Escobar *et al.*, who demonstrated an insignificant difference in serum CRP levels between chronic periodontitis patients and healthy participants, and they suggested that the inflammatory response was only local(16). However, a study by Craig *et al.* suggested that periodontal disease is associated with an increased serum level of CRP, which contrasts with the results of the present study (17).

A study conducted by Moghadam *et al.* also revealed an association between elevated CRP serum levels and chronic periodontitis, contrasting the present study.

The study observed that the increase in serum CRP levels was associated with the severity of the periodontal disease after adjusting for Body Mass Index, age and smoking (18).

The present study found that smoking without periodontal disease is not significantly associated with elevated CRP serum levels when comparing healthy non-smokers (group A) with healthy smokers (group C). This finding is consistent with Aldaham*et al.,* who did not find any significant difference in CRP levels between smokers and former smokers. However, they stated that smoking status was associated with a significant increase in IL-6 levels (19).

A study in contrast to present one, conducted by Gazy*et al.,* compared four equal groups; Non-smokers with clinically healthy periodontium (GI); Smokers with clinically healthy periodontium (GII); Non-smoker with CP (GIII), and Smoker with CP (GIV), reported that smoking led to significantly higher salivary CRP (20).

The present study demonstrated that smoking had no impact on the CRP serum levels of chronic periodontitis participants as revealed by the statistically insignificant differences between healthy non-smoker participants in (group A) and the smokers with chronic periodontitis in (group D).

The results of the current study are also in contrast to the studies of Waseem*et al.*, Raval*et al.* and Azizi *et al.* which indicated that the combination of smoking and periodontal disease could increase the CRP serum levels. These studies concluded that the highest level of CRP was found in smokers with periodontitis, followed by non-smoker periodontitis patients and smoker non-periodontitis patients. Former smokers had a minimum of CRP compared to the other groups (21–23).

In conclusion, the findings of the study showed that elevated CRP serum levels are not associated with inflammatory periodontal disease nor smoking, and nor is it associated with the combination of periodontal disease and smoking.

However, the findings highlight the need to conduct large-scale longitudinal interventionalstudies to clarify the relationship between the combination of periodontal disease, smoking and CRP serum levels and to investigate other inflammatory markers such as IL-6, TNF-α that could have added to the inflammatory burden of the individual that may increase the risk of cardiovascular eve

The cross-sectional study design may have prejudicedthe findings toward the null hypothesis, that it does not allow for conclusions to be made regarding causality. Also, all participants were recruited only from the Khartoum Dental Teaching Hospital; which limited the ability to apply the findings to the general population. Furthermore, the present study was only a short- term study

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