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Level of Plasma Prostaglandin-Endoperoxide Synthase 2 (PTGS2) in Patients with Chronic Periodontitis and its Correlation with Clinical Periodontal Parameters.

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ABSTRACT

Background: Periodontitis is a destructive chronic inflammatory disease causing irreversible loss of tooth-supporting tissues. Prostaglandin-endoperoxide synthase 2 (PTGS2) is an important inflammatory mediator that is overexpressed in periodontitis as well as other diseases. Periodontitis may contribute to an elevated plasma PTGS2 level.

Aims: To determine the level of PTGS2 in the plasma of chronic periodontitis patients in comparison to periodontally healthy controls. Also to investigate whether there is any correlation between PTGS2 plasma levels and clinical periodontal parameters.

Methods: Blood samples were collected from 60 chronic periodontitis (CP) cases (moderate to severe periodontitis) and 60 periodontally healthy controls. A questionnaire was used to collect information from each participant. Clinical Periodontal parameters were recorded. Blood samples were collected in EDTA containing tubes and centrifuged to obtain plasma samples which then were frozen at -70c. ELISA was performed to determine the PTGS2 level in the plasma samples.

Results: The mean clinical attachment loss (CAL) was 4.35mm in the CP cases. ELISA analysis showed a statistically significant elevation of PTGS2 concentration in the plasma of periodontitis cases compared to controls (p=0.001). However, the Person correlation coefficient revealed a negative correlation between PTGS2 plasma concentration and the clinical periodontal parameters in both cases and control groups.

Conclusion: Periodontitis may contribute to elevated plasma levels of PTGS-2 whose elevation is related to other diseases such as osteoarthritis, atherosclerosis, proliferative diseases, and preterm delivery. However, longitudinal studies and intervention trials are needed before any causative role can be assigned.

Keywords: chronic periodontitis, plasma prostaglandin-endoperoxide synthase 2, correlation.

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INTRODUCTION

Periodontitis is an inflammation of the periodontal tissues that results from the extension of untreated gingivitis in susceptible individuals.[1] Although microbial plaque is the primary cause of periodontal diseases, host inflammatory and immune response is responsible for most of the tissue destruction and bone resorption seen in periodontitis.[2] Genetic and environmental factors determine the nature of the inflammatory response which is essential in determining disease progression.[3,4] Prostaglandin-endoperoxide synthase 2 (PTGS2) is an effective inflammatory mediator in the pathogenesis of periodontitis, it converts arachidonic acid to prostaglandins (PGs) and mainly prostaglandin E2 which mediates inflammation and stimulates osteoclastogenesis and bone resorption. PTGS2 secretion is induced by pro-inflammatory cytokines.[5,6] It is overexpressed in inflamed tissues and correlated to the degree of tissue destruction and periodontal attachment loss.[7] Inflammatory mediators that are locally increased in the periodontal tissues of periodontitis patients could be also elevated in the plasma of those patients,[8] thereby periodontitis may contribute to an elevated plasma PTGS2 concentrations which increases the susceptibility of periodontitis patients to other PTGS2 related chronic inflammatory diseases and adverse pregnancy outcomes.

MATERIALS AND METHODS

For this study, 120 subjects were recruited; 60 chronic periodontitis patients (31 males and 29 females) with age range from 35to 55 years, and 60 healthy controls (32 males and 28 females) with age range from 30 to 51 years.

Informed consent was obtained from each participant, and a questionnaire was used to record the background information and dental and medical histories of the participants.

Periodontal status was examined and clinical periodontal parameters including plaque index, gingival index, bleeding on probing, probing pocket depth and clinical attachment level were recorded for the participants and accordingly the participants were assigned either to chronic periodontitis group or control group.

Chronic periodontitis patients were diagnosed according to the criteria made by the international workshop for classification of periodontal diseases and conditions.[9]

Subjects who were excluded from the study included: patients with Systemic diseases like diabetes, immunosuppressive disorders, bleeding disorders and any other disease which may affect the progression of periodontal disease; pregnant and lactating women; Tobacco smokers and subjects currently on antibiotics and/or anti-inflammatory medication or any other medication known to affect the periodontium or have used them within the last 3 months.

3 ml of venous blood was collected from each participant by venipuncture and transferred into Ethylene diamine tetraacetic acid (EDTA) containing tubes. The tubes were centrifuged for 10 minutes at 1000rpm to obtain plasma samples which then were frozen at -70c. ELISA analysis was

performed using the plasma samples according to the manufacturer's instructions. The procedures were as follows: 100 µl of the standard solutions and each plasma sample were pipetted into a 96-well plate provided. The plate was covered and incubated for 1.5 h, then washed with washing buffer twice and dried. 100 µl of the previously prepared biotinylated antibody liquid was added into each well and incubated at 37 for 1 h, then the plate was washed 3 times and dried. 100 µl of the previously prepared enzyme conjugate liquid was added into each well and incubated at 37°C for 30 minutes, then the plate was washed 5 times and dried. 50 µl of the previously prepared colour reagent A then B were added into each well then the plate was shaken and incubated for 10 minutes at 37°C away from light for colour development. 50µl Stop Solution was added to each well to stop the reaction. The plate was read at 450 nm wavelength using Universal Microplate Reader. The level of PTGS2 in each sample was obtained by comparison with the standard curve generated from standards supplied by the manufacturer.

Statistics Package for Social Science (SPSS, version 22) was used to perform statistical analysis. Both descriptive and analytical statistics were used. The statistical significance of difference between means was calculated by t-test. Differences were considered significant when the probability value $p<0.05$. Pearson's correlation coefficient (r) test was used to test the correlation between plasma PTGS2 concentration and clinical periodontal parameters.

RESULTS

Characteristics of the study subjects (healthy controls and periodontitis cases) are shown in table 1. The mean age (±SD) was 39 (±7.03) years for controls, and 47 (±6.95) years for periodontitis cases. The male: female ratio was 63:57 (32:28 in the control group and 31:29 in chronic periodontitis group).

The clinical periodontal parameters of the chronic periodontitis cases and controls are shown in table 2. The mean PLI and GI for cases vs controls were (1.98 (±0.25) vs 0.64 (±0.18) and 1.65 (±0.29) vs 0.52 (±0.13) respectively. The mean values of BOP%, PPD and CAL for periodontitis cases were (63.79% (±29.8), 2.96 (±0.63) and 4.35 (±0.94) respectively.

ELISA analysis revealed a statistically significant difference in the concentration of PTGS2 in the plasma of periodontitis patients compared to periodontitis free controls (129.34 pg/ml for cases and 80.72 pg/ml for controls, $p=0.001$), (Table 3).

The results showed a weak negative correlation between plasma PTGS2 and clinical periodontal parameters in both periodontitis patients and controls with a significant negative correlation between plasma PTGS2 and PLI in the control group, (Table 4).

DISCUSSION

Periodontitis is a multifactorial inflammatory disease initiated by bacterial plaque accumulation.[10] Most of the tissue destruction in periodontitis is attributed to the inflammatory response itself rather than to the microorganisms in dental plaque.[11] PTGS-2 plays a crucial role in the inflammatory response via stimulating the production of prostaglandins, especially prostaglandin E2 (PGE2), the potent inflammatory mediator and osteoclastogenesis stimulator.[12,13] Previous studies have revealed an overexpression of PTGS-2 and increased production of PGE2 in periodontal tissues of patients with periodontitis compared to healthy controls.[13-15] The effect of systemic conditions on periodontal disease has been investigated for many years. However, recent studies have been focusing on the impact of periodontitis on systemic health. These studies try to find out whether periodontitis increases the risk for systemic diseases and conditions such as low birth weight (LBW) delivery, diabetes, cardiovascular and cerebrovascular diseases, and respiratory diseases.[16-19] Such a relationship between periodontitis and systemic diseases could be explained by the fact that microorganisms from a periodontal pocket could reach other parts of the body through the bloodstream. Furthermore, the inflammatory mediators which are released in response to plaque bacteria might cause systemic challenge.[8,20,21] In the current study, it has been shown that PTGS2 concentration is significantly elevated in the plasma of periodontitis patients compared to controls. Elevated PTGS2 concentration has been also related to other diseases such as osteoarthritis, atherosclerosis, proliferative diseases, and low birth weight delivery.[22,23]

CONCLUSION

Periodontitis may contribute to elevated plasma levels of PTGS-2, hence, periodontitis might increase the susceptibility to other PTGS2 related diseases. However, longitudinal studies and intervention trials are needed before any causative role can be assigned.

CONFLICT OF INTEREST

None

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Table 1: Characteristics of the study subjects

Characteristics		groups CASES (N=60)	CONTROLS (N=60)	Total N=120
Mean age		47 (±6.95) years	39 (±7.03) years	-
Gender	Female	29	28	57
	Male	31	32	63

N: number

Table 2: Clinical Periodontal Parameters.

Groups	Mean values (±SD)				
	PLI	GI	BOP%	PPD	CAL
CP cases	1.98 (±0.25)	1.65 (±0.29)	63.79% (±29.8)	2.96 (±0.63)	4.35 (±0.94)
Controls	0.64 (±0.18)	0.52 (±0.13)	-	-	-

CP: chronic periodontitis, PLI: plaque index, GI: gingival index, BOP: bleeding on probing, PPD: probing pocket depth, CAL: clinical attachment loss, SD: standard deviation.

Table 3: Comparison of the mean plasma PTGS2 concentration between study groups

	Groups	Mean values (±SD)	Df	T-test	P-value
PTGS2(pg/ml)	CP cases	129.34 (±111.69)	118	24.68	0.001
	Controls	80.72 (±72.38)			

PTGS2: Prostaglandin-endoperoxide synthase 2.

Table 4: Correlation between plasma PTGS2 and clinical periodontal parameters in cases and controls

	Groups	STATISTICAL ANALYSIS	PLI	GI	POB	PPD	CAL
PTGS2	CASES	r	-0.151	-0.133	-0.106	-0.240	-0.252

	P-value	0.251	0.310	0.421	0.065	0.052
CONTROLS	r	-0.272*	-0.220			
	p-value	0.035	0.092			

r: person correlation, PLI: plaque index, GI: gingival index, BOP: bleeding on probing, PPD: probing pocket depth, CAL: clinical attachment loss, * Statistically significant ($p<0.05$).

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