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Correlation of Serum Tumor Necrosis Factor Alpha and High Sensitive C-Reactive Protein with Clinical Periodontal Parameters in Osteoarthritis Patients.

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ABSTRACT

Periodontitis (PD) is an inflammatory disease of thesupporting tissues of the teeth which is caused by specific microorganisms and characterized by extensive destruction of periodontal ligament and alveolar bone with pocket formation, gingival recession or both. A total of 80 subjects in both sexes aged (35 to 50) years first group 30 patients with osteoarthritis and moderate chronic periodontitis, second group 30 patients in both sexes aged (35 to50)years with moderate chronic periodontitis alone. And control group of 20 healthy patient with healthy periodontitium participate in this cross sectional study. we excluded the postmenopausal and pregnant woman from female patients and smoker patient also. All patients are free of medication. All subjects are in good general health with no history of systemic disease. Participants with OA have documentation or radiographic imaging, consistent with degenerative arthritis in the absence of an inflammatory condition. taking the clinical periodontal parameters which include :Plaque Index (PI), Gingival Index (GI),bleeding on Probing (BOP), Probing Pocket depth (PPD), Clinical Attachment Level (CAL).Venous blood samples are drawn from each subject. using pyrogen-free heparinized collection tubes. Tubes are centrifuge according to the manufacturer's guidelines, then stored at _15C till analyze. serum TNFα and hsCRP will be measure using an enzyme-linked immunosorbent assay (ELISA). Patients with moderate chronic periodontitis and osteoarthritis had higher median of dental plaque, gingival inflammation, and no significant difference in probing depth, bleeding on probing and attachment loss compared to those who had chronic periodontitis only. There is no correlation between TNFα , hsCRP and clinical periodontal parameters in patients with osteoarthritis.

Keywords: chronic periodontitis, osteoarthritis, TNFα, hsCRP.

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INTRODUCTION

Periodontal disease is an infectious disease of the oral cavity initiated by Gram-negative bacteria, characterized by inflammatory cell accumulation in the periodontal tissues. (1) It results from the interaction between bacteria's existence in the biofilm of plaque and the immune response of the host body. Periodontitis is one of disease types, leading to destroy periodontium or the tooth supporting structures including the periodontal ligament and the alveolar bone.(2) Periodontitis can affect the masticatory function and aesthetics, cause to tooth loss, which not only decreases the quality of life but also negatively causes acquired systemic disease. Osteoarthritis (OA):The most common chronic and currently regarded as potentially irreversible disease that affects the joints(3,4). The constantly growing number of causes for the development of the disease includes, for example, genetic predisposition, aging, obesity, trauma, and other systemic diseases.. According to the latest medical knowledge, the participation of the immune system in the development and progression of OA is one of the key elements in the pathogenesis of the disease (5).

Also it is a chronic joint disease have compound etiologies characterized with synovial inflammation, remodeling of subchondral bone, and produce osteophytes, which in turn cause cartilage deterioration, severity of osteoarthritis afflicted functional ability. (5). Hence, osteoarthritis in most of people leading to incapable or maintain proper oral hygiene, lead to accumulation of plaque and calculus, which increases hazard of dental caries and periodontal disease(6).Cytokines are biologically active molecules released by specific cells that elicit a particular response from other cells on which they act ,they are effective in very low concentrations, are produced transiently, act locally in the tissue where they are produced .They act as a communication between immune and non immune cells(7). It has been projected that cytokines are necessary to the pathogenesis of many diseases (8). C-reactive protein is a systemic marker during the acute phase of an inflammatory response released. C-reactive protein is produced by the liver and is regulated by circulating cytokines, such as tumor necrosis factor and interleukin- 1, from local and or systemic inflammation like as periodontal inflammation(9). Tumor necrosis factor-alpha (TNFα) is an critical of pro-inflammatory mediator that result in destruction of periodontal tissues. TNFα has a many of actions, mostly pro-inflammatory. Leukocyte recruitment and vascular permeability are facilitated by stimulating expression of selectins and adhesins by TNFα, activating the osteoclasts similarly to way with IL- lead toresorption of bone and extracellular matrix. Monocytes and macrophages are the most important cell types producing TNF-α (10). these cytokines are noramally found in the blood and increase with inflammation so in this study we determine clinical periodontal parameter and correlate with TNF alpha and hsCRP in each group.

MATERIALS AND METHODS

Sample population consisted of eighty males and females subjects with age range (35-50)years. moderate chronic periodontitis with osteoarthritis (CP+OA) group (30) subject were seeking the rheumatology clinic in Baghdad Teaching Hospital, and the chronic periodontitis (CP) groups (30)subject, with control (C) group (20)subject were recruited from the attendants to Iraqi National Blood Bank. The people enrolled voluntarily in the study in the period between December, 2016 – March, 2017, they were subjected to a questionnaire including question their name, age, full medical history, dental history, medications. Then dignosed and examined for clinical periodontal parameters(plaque index PI,gingival index GI,bleeding on probing BOP,periodontal poket PPD and clinical attachment lossCAL) Followed by blood collection for the assessment of serum level of TNFα and hsCRP.

Exclusion criteria: Pregnant and menopause ladies, smokers, any patient had history of other chronic systemic diseases with known associations with CP as cardiovascular diseases and diabetes mellitus.Also Rheumatoid patient and Periodontitis patient who received periodontal treatment and /or antibiotics during the last 3months.

Collection of blood Samples: After the subjects have been selected five ml of venous blood sample were aspirated from anticubital vein of each individual, using disposable plastic syringes with 23 gauge stainless steel needle. The whole blood was collected in sterile disposable plain tubes. After collection of the whole blood, centrifuging at(2000-3000)rpm for 20 minutes.Aspirated and transferred immediately into anothertube and frozen at (-15 C) for subsequent analysis. Haemolyzed samples were discarded.Then The ELISA kit uses Sandwich-ELISA as the method. The Microelisastripplate provided in this kit has been pre-coated with an

antibody specific toTNF α and hs-CRP. Standards or samples are added to the appropriate Microelisastripplate wells and combined to the specific antibody.

Statistical Analysis: Each patient assigned a serial identification number. The data were reviewed, cleaned with double check entry into the computer using Statistical Package for Social Sciences (SPSS) version 21. The overall comparison of mean values among the different study groups was done by Kruskal–Wallis .A Comparison between any two study groups was done by Mann–Whitney U-test. The correlation between TNF-α, hs CRP and the clinical variables in each group was done by Spearman's correlation test.

RESULTS

In table (1)showed that both median and mean rank of PL were higher among CP+OA group (1.599, 52.82) than other the two groups as ,CP group (1.40, 48.18) and the control group (0.271, 10.50) with highly significant difference between these groups P<0.01) .And in table (2) showed that both median and mean rank of GL were higher among CP+OA group (1.200, 55.32) than other two groups as CP group (0.900,45.68) and the control group (0.120, 10.50) with highly significant difference between these groups (P<0.01),in table(3) showed that both mean and mean rank of BOP score1 was higher in chronic periodontitis CPgroup(11.612,32.57)than chronic periodontitis with osteoarthritis (CP+OA) group(10.821,28.43) with not significant difference between these two groups P>0.05,The result shown in table (4) the higher median and mean rank of PPD was in CP+OA group(1.250,31.38)while the median and mean rank of CP only was(1.200,29.62) and it was not significant difference between two groups P>0.05.The result in table(5) show that the higher median and mean rank of clinical attachment loss (CAL) in CP group was(2.800,31.40) while the median and mean rank in CP+OA group was (2.650,29.60) and the result was stastically not significant difference P>0.05.

There is weak non significant correlation between TNFα, hsCRP and clinical periodontal parameters. Table 6.

Table 1: Descriptive and statistical test of PL among groups

Group	Min.	Max.	Mean	±SD	Median	Mean Rank	Kruskal-Wallis#	
							X2	Sig.
Control	0.03	0.380	0.251	.093	0.271	10.50	45.15	0.000 HS
CPonly	0.80	2.500	1.525	.498	1.400	48.18		
CP+OA	0.70	2.500	1.625	.487	1.599	52.82		

Table2: Descriptive and statistical test of GI among groups

Group	Min.	Max.	Mean	±SD	Median	Mean Rank	Kruskal-Wallis#	
							X2	Sig.
Control	.018	.295	.132	.083	0.120	10.50	47.151	0.000 HS
CPonly	.600	2.000	1.068	.400	.900	45.68		
CP+OA	.500	2.200	1.303	.464	1.200	55.32		

Table 3: Descriptive and statistical tests of BOP score (1) among groups

Group	Min.	Max.	Mean	±SD	Median	Mean Rank	Mann-Whitney U test		sig
							Z	P-value	NS
CP. Only	7.400	18.500	11.612	2.892	10.320	32.57	0.917	0.359	
CP+OA	5.200	18.700	10.821	3.640	10.350	28.43			

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Table 4: Descriptive and statistical test of PPD among groups

Group	Min.	Max.	Mean	±SD	Median	Mean Rank	Mann-Whitney U test		Sig
							Z	p-vaue	NS
CP. Only	1.000	6.300	1.960	1.608	1.200	29.62	0.396	0.692	
CP+OA	1.000	6.400	2.791	2.065	1.250	31.38			

Table5: Descriptive and statistical test of CAL between groups

Group	Min.	Max.	Mean	±SD	Median	Mean Rank	Mann-Whitney U test		Sig
							Z	p-value	
CP. Only	1.400	4.100	2.828	.686	2.800	31.40	0.400	0.689	NS
CP+OA	1.400	4.100	2.744	.615	2.650	29.60			

Table 6: The correlation of TNFα, hsCRP and clinical periodontal parameters

Groups	Variables	R	P-value
Control	PLI	-.310	.184
	GI	-.303	.193
CP	PLI	.074	.698
	GI	.227	.228
	BOP1	.090	.635
	BOP0	-.090	.635
	PPD	-.018	.927
	CAL	.354	.055
CP+OA	PLI	.137	.470
	GI	.214	.256
	BOP1	.203	.282
	BOP0	-.201	.286
	PPD	-.093	.625
	CAL	-.012	.949

DISCUSSION

The present study reported that there is a high significant difference in the median values of gingival index and Plaque index in the OA+CP group. This elevation of GI and PLI reflects a higher inflammation in the chronic periodontitis associated osteoarthritis than the chronic periodontitis (CP) group and could be related to limitation of patient movement which hinder oral hygiene practices lead to bacterial aggregation ,formation of microbial bio-_film (plaque)and bacterial invasion with its toxin which result in disruption of the epithelial barrier and more destruction to the supporting tissue this increase the exposed area for plaque accumulation on tooth surface (carrenza 2012) , This result is agreed with Powers et al.(11) which approved that patient with osteoarthritis had higher mean of GI .and disagree with Torkzaban et al.(12)which found that no significant correlation was evident between OA and the mean percent of GI. reason for this finding is that the status of oral hygiene was poor (GI>50%) among all subjects with and without OA. Therefore, the difference between the two groups was not statistically significant. Although The percentage of sites with BOPscore 1 was higher in OA+CP group than CP group but the difference was non significant which agree with the study of Chung et al.,(13).This may be attributed to the effect of plaque accumulation on the pathophysiololgic process and blood circulation in the inflamed tissue and the severity of bleeding correlated with the intensity of inflammation (carrenza2012).Unfortunately there is no further studies before to compare with our result.

Periodontal pockets vary in their location and depth; hence changes in the mean probing depths for the entire mouth provide reasonable information accordingly to this study, PPD was higher in OA+CP group than CP group but statistically was no significant difference between the study groups. This agree with Chung

et al.(13)who found CP+ OA and CP showed no significant association in overall analysis according to clinical periodontal parameters .the increasing in pocket depth may be contributed to increase amount of plaque and bacterial invasion with its toxin which cause further destruction in sulcular and junctional epithelial ,alveolar bone tissue and other supporting tissue .

Clinical attachment level refers to the distance from the cemento enamel junction (CEJ) to the location of the inserted probe tip. Thus, loss of fibers attachment expressed at the clinical level the cumulative effect of destructive pathological processes in periodontal disease ,in our study show no significant difference between OA+CP group and CP group this was also agree with Chung et al(13)which found that there is no stastically difference between the two groups , the osteoarthritis have no effect on the clinical periodontal parameters which found no significant difference except for plaque and gingival index which may be related to patient's poor ability to maintain proper oral hygiene may result in accumulation of plaque and calculus.

So it was clear that their levels increased in osteoarthritis and periodontal disease but in our study statically the difference was non-significant which may be related to the newly dignosed disease, osteoarthritis is a non-inflammatory disease, and the proinflammatory TNFαlevel is stillless in the serum of the patient and may be the severity of periodontitis was moderate effect on the destruction of the supporting tissue so affect little on the inflammatory markers in the serum.

In this study we found almost a weak negative correlation between TNFα,CRP and clinical periodontal parameters in each group .

Our conclusion of this study (TNFα,hsCRP)showed no correlation with clinical periodontal parameters. Prospective research and studies using clinical criteria for diagnosis of symptomatic OA are needed to confirm these findings.

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