International Journal of Advanced Research in Biological Sciences
ISSN: 2348-8069
www.ijarbs.com
DOI: 10.22192/ijarbs Coden: IJARQG(USA) Volume 3, Issue 9 - 2016

Research Article

DOI: 10.22192/ijarbs.2016.03.09.004

Salivary Biomarkers (PGE2, MMP-8, ALP Levels) and Clinical Periodontal Parameters for Segregation of Periodontal Health and Diseases

Amel O. Hassan[*], Saad M. Hussein[*], Wisam W. Sahib

[*]Department of Physiology, College of Medicine, Babylon University /Iraq
*Corresponding author: *zainaldeen822@gmail.com*

Abstract

Periodontal Diseases (PD) are the common inflammatory diseases of the structures around the teeth including gingiva, periodontal ligament and alveolar bone. Gingivitis and periodontitis are the major groups of PD. This is study conducted on a total 80 subjects; 29 (12 female &17 male) gingivitis patients, 27 (11 female & 16 male) chronic periodontitis patients and 24 (15 female &9 male) as a control subjects. Unstimulated whole saliva samples were collected to determine the levels of PGE2, MMP-8 and ALP. Clinical periodontal parameters were recorded at four sites per tooth. The study founded the prevalence of gingivitis and chronic periodontitis higher in males than females. On the other hand, the present study findings revealed a highly significant difference among the three studies groups for all of clinical periodontal parameters and salivary biomarkers parameters. The present study showed a significant and highly significant positive correlation between each of salivary biomarker level and all of clinical periodontal parameters and between salivary biomarkers parameters.

Keywords: Prostaglandin E2, matrix metalloproteinase-8, alkaline phosphatase, gingivitis and chronic periodontitis.

Introduction

Periodontal diseases (PD) are inflammatory diseases that affects the soft and hard structures (periodontium) that support the teeth. (Mutamuliza, *et al*., 2015). PD are graded among the ten most prevalent chronic diseases worldwide, and considered as a main public health problem (Gustavo, *et al*., 2014). Periodontal diseases can be broadly divided into two major categories: gingivitis and periodontitis (Taylor, 2014). Gingivitis, in which the inflammation is superficial, restricted to the gingiva tissues (gum). (Leong, *et al*., 2014). While periodontitis is considered as the chief cause of tooth loss. The most common form of periodontitis is the chronic periodontitis. (Chrzeszczyk, *et al*., 2015). The presence of plaque biofilm that colonize the supra and sub gingival area of tooth and the imbalance between host immune response and periodontaopathic bacteria is considered the most common cause of PD (Carinci, *et al*., 2015). Conventional clinical periodontal parameters measurement such as gingival index (GI), plague index (PLI), bleeding on probing (BOP), probing pocket depth (PPD) and clinical attachment loss (CAL) are used for periodontal diseases diagnosis of pervious periodontal disease rather than present diseases activity (Kongkhunthian, *et al*., 2014). Saliva is the mirror of body, it is of great help in detect, and diagnosis of PD (Pakngad & Rezaaei, 2013). The main motive given for the utilize of saliva as a diagnostic tool is that the majority of biomarkers found in blood, urine and other body fluids may also be present in

saliva samples (Rocha, *et al*., 2013). Prostaglandin E2 (PGE2) is pro-inflammatory cytokines synthesis from cell membrane phospholipids. It is pondered a key inflammatory mediator in PD and related with periodontal disease progression. (Camargo, *et al*., 2015). Salivary matrix metalloproteinase-8 (MMP-8) is a major factor produced by neutrophils at sit of inflammation so it serve as a good biomarker of PD and aid in early detection of gingivitis and periodontitis (Gupta, *et al*., 2015). The Alkaline Phosphatase (ALP) is intracellular enzyme released by many cells within the area of the periodontium and gingival crevice in periodontal tissues inflammation and destruction (Luke, *et al*., 2015).

The aims of the present study were:

1. To determine the periodontal health status in studies groups by measuring clinical periodontal parameters (PLI, GI, BOP, PPD and CAL).

2.To estimate the salivary levels of biochemical markers (PGE2, MMP-8 and ALP).

3. To determine the correlation between clinical periodontal parameters and salivary biomarkers.
4. To determine the correlation between salivary biomarkers parameters.

Materials and Methods

Sample population included eighty subjects of both males and females aged from 30 to 50 years old. The subjects enrolled in the present study were from the attendants to the clinic of the department of periodontology in Specialist Center for Dentistry in Babylon City / Iraq. The subjects divided according to the international classification system of American Academy of Periodontology (AAP) for periodontal disease in 1999 (Lang, *et al*., 1999). Into three groups (control, gingivitis and chronic periodontitis), based on clinical examination according to GI, BOP, PPD and clinical CAL.

Methods:

1. Saliva collection:

After the subjects have been selected and before the clinical periodontal parameters examination, the whole unstimulated saliva samples were collected between the hours of 9-11 a.m. Within at least one hour before the sample collection, the subject must not eat or drink anything except water. Each subject was asked to rinse his mouth thoroughly with water to insure the removal of any debris, then waiting for 1-2 min for water clearance. The subject should sit in a relaxed position, with tilt their heads slightly forward, and rest for 5 min (Rahim, 1998). Five ml of unstimulated whole saliva was collected from each subject (Tenovuo & Lagerlof, 1994). Saliva then putted in small cooling box to stop the growth of bacteria. After that, the saliva centrifuged and frozen until being analyzed. (Gronbland, 1998).

2. Clinical periodontal parameters examination:

PLI, GI, BOP, PPD and CAL was performed by using Michigan O periodontal probe on four surfaces (mesial, buccal/ labial, distal and lingual/ palatal) of all teeth except third molar, all subjects must have at least 20 teeth.

PGE2 and MMP-8 were done by Enzyme Linked Immuno-Sorbent Assay (ELISA) technique by using kit manufactured by Elabscience, China. While ALP was done by Colorimetric method by using kit manufactured by Biolabo, France.

Results

1. Gender Distribution:

In this study founded the males more affected with periodontal diseases (gingivitis and chronic periodontitis) than females. The percentage of males (58.62 %, 59.25%) higher than females (41.37 %, 40.74%)) in gingivitis and chronic periodontitis respectively as shown in figure (1).

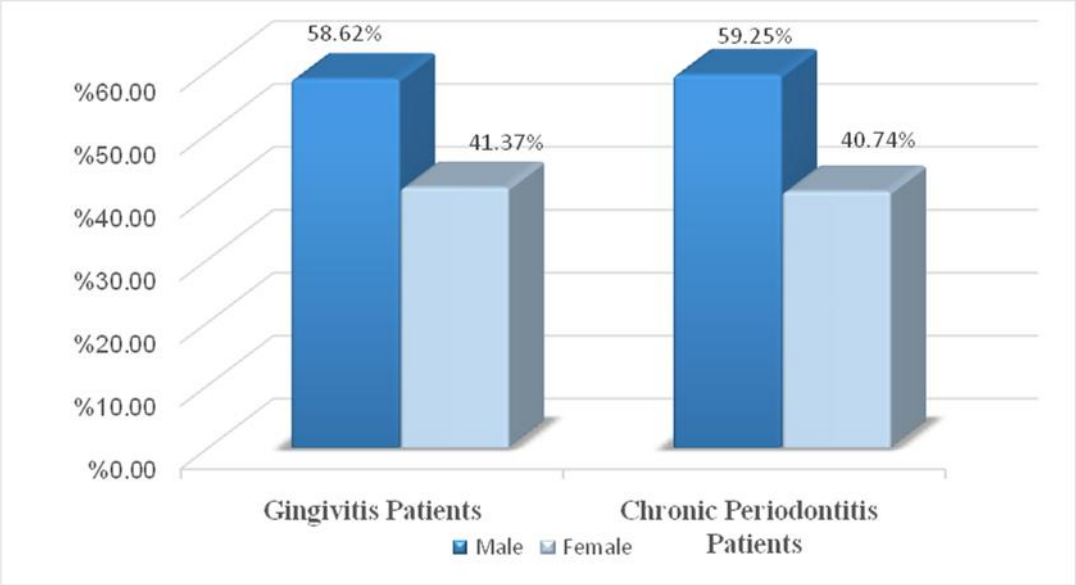

Figure (1): Gender distribution of gingivitis and chronic periodontitis groups

2. Descriptive of Clinical Periodontal Parameters:

Clinical periodontal parameters for the study groups were summarized in table (1). The mean ±SD value of the PLI and GI among the control, gingivitis and chronic periodontitis groups. In addition, the mean ± SD values of BOP, PPD and the CAL between gingivitis and chronic periodontitis patients groups since there is no BOP, PPD and CAL in control group. It was clearly shown that chronic periodontitis group presented the higher mean value followed by gingivitis group and lastly the control group showed the minimum mean value. Group comparison among control, gingivitis and chronic periodontitis groups showed that there was a highly significant difference ($P < 0.01$).

Table (1): ANOVA Test of clinical periodontal parameters among the control, gingivitis and chronic periodontitis groups.

Variable / Group	PLI	GI	BOP%	PPD	CAL
Control group	0.46±0.15	0.36±0.04	0	0	0
Gingivitis group	1.05±0.26	1.31±0.28	23.07±2.55	2.21±0.30	0.55±0.26
Chronic periodontitis group	1.78±0.40	1.75±0.36	42.15±4.96	4.45±0.97	5.34±0.74
p-value	0.001	0.001	0.001	0.001	0.001

Highly significant difference ($P < 0.01$).

3. Descriptive of Salivary Biomarkers Parameters:

The study had revealed that there is a highly significant difference ($P< 0.01$) in salivary [PGE2 levels (pg/ml), MMP-8 levels (ng/ ml) and ALP levels(IU/ L)] among the studied groups. Chronic periodontitis group presented the higher mean value of salivary biomarkers followed by gingivitis group and lastly the control group showed the lowest mean value as shown in table (2).

Table (2): ANOVA Test among Variables of Prostaglandin E2, Matrix Metalloproteniase-8 and Alkaline Phosphatase for control, gingivitis and chronic periodontitis groups.

Variables	Control group Mean ± SD	Gingivitis group Mean ± SD	Chronic periodontitis group Mean ± SD	p-value
Prostaglandin E2 (PGE2) pg/ ml	195.56± 102.35	653.92± 145.64	1085.49± 97.68	0.001
MatrixMetalloproteinase-8 (MMP-8) ng/ ml	137.14± 27.91	237.20± 28.07	366.75± 32.20	0.001
Alkaline Phosphatase (ALP) IU/ L	6.60 ± 3.39	19.81 ± 3.77	32.61 ± 7.27	0.001

Highly Significant P<0.01

4. Correlation of Prostaglandin E2 (PGE2) levels (pg/ml)with clinical periodontal parameters:

In table (3) there was a significant positive correlation (P< 0.05) and a highly significant positive correlation (P< 0.01) between PGE2 levels (pg/ml) and clinical periodontal parameters in gingivitis and chronic periodontitis groups.

Table (3): Pearson's Correlation Coefficient of Clinical periodontal Parameters with PGE2 levels (pg/ ml) in gingivitis and chronic periodontitis Patients groups.

PGE2 (pg/ml)		Clinical periodontal parameters				
		PLI	**GI**	**BOP%**	**PPD**	**CAL**
Gingivitis group	**r**	0.582	0.576	0.629	0.567	0.638
	p-value	0.029	0.031	0.016	0.023	0.017
Chronic periodontitis group	**r**	0.537	0.454	0.689	0.841	0.815
	p-value	0.031	0.017	0.001	0.001	0.001

Highly Significant P<0.01, significant difference P< 0.05

5. Correlation of Matrix Metalloproteinase-8 (MMP-8) Levels (ng/ml) with Clinical Periodontal Parameters:

There was a significant positive correlation (P< 0.05) and a highly significant positive correlation (P< 0.01) between MMP-8 levels (ng/ml) and clinical periodontal parameters in gingivitis and chronic periodontitis group was shown in table (4).

Table (4): Pearson's Correlation Coefficient of Clinical periodontal Parameters with MMP-8 levels (ng/ ml) in gingivitis and chronic periodontitis Patients groups.

MMP-8 (ng/ml)		Clinical periodontal parameters				
		PLI	**GI**	**BOP%**	**PPD**	**CAL**
Gingivitis group	**r**	0.474	0.770	0.570	0.485	0.582
	p-value	0.014	0.001	0.027	0.022	0.019
Chronic periodontitis group	**r**	0.546	0.689	0.847	0.736	0.841
	p-value	0.013	0.006	0.001	0.001	0.001

Highly Significant P<0.01, significant difference P< 0.05

6. Correlation of Alkaline Phosphatase (ALP) Levels (IU/L) with Clinical Periodontal Parameters:

The results of this study showed a significant positive correlation (P< 0.05) and a highly significant positive correlation (P< 0.01) between ALP levels (IU/L) and clinical periodontal parameters in gingivitis and chronic periodontitis patients groups as shown in table (5).

Table (5): Pearson's Correlation Coefficient of Clinical periodontal Parameters with ALP level (IU/ L) in gingivitis and chronic periodontitis Patients groups.

ALP (IU/ L)		Clinical periodontal parameters				
		PLI	GI	BOP%	PPD	CAL
Gingivitis group	r	0.404	0.408	0.499	0.530	0.543
	p-value	0.039	0.040	0.038	0.023	0.020
Chronic periodontitis group	r	0.635	0.431	0.553	0.760	0.832
	p-value	0.011	0.031	0.033	0.001	0.001

Highly Significant P<0.01, significant difference P< 0.05

7. Correlation among Salivary Biomarkers Parameters (PGE2, MMP-8 and ALP Levels):

This study illustrated a highly significant positive correlation (P< 0.01) between PGE2 and MMP-8 levels in gingivitis and chronic periodontitis groups. Additionally this study showed a significant positive correlation (P< 0.05) between PGE2 and ALP levels and between MMP-8 and ALP levels in gingivitis and chronic periodontitis groups as explained in table (6).

Table (6): Pearson's Correlation Coefficient between each two of salivary biomarkers PGE2, MMP-8 and ALP levels in gingivitis and chronic periodontitis Patients groups.

Variables	Gingivitis group		Chronic periodontitis group	
	R	p-value	r	p-value
PGE2 and MMP-8	0.760	0.001	0.832	0.001
PGE2 and ALP	0.487	0.013	0.570	0.027
MMP-8 and ALP	0.472	0.021	0.549	0.030

Highly Significant P<0.01, significant difference P< 0.05

Discussion

Gender:

In the present study, the prevalence of the periodontal diseases was revealed higher in male subjects. Hence the results in this study appeared accordance with (Baser, *et al*., 2014). The possible reason for these gender differences, the females possess greater interest in oral health and perceive their oral health to be good to a higher degree than males. The males have less positive attitudes towards oral health and dental-visit behavior.

Clinical Periodontal Parameters Finding:

The present study revealed a highly difference (P< 0.01) elevation of mean values of PLI, GI, BOP, PPD and CAL indices among the control, gingivitis and chronic periodontitis groups. In the table (1), the results of clinical periodontal parameters finding in this study agreement with (Khongkhunthian, *et al*., 2014).

The increase mean value of PLI explain the role of the pathogen in the development and severity of PD. This is clear since plaque is the chief etiological factor in PD and are supported by the fact that the microbial biofilm is considered the primary and the major

etiological factor responsible for initiation of periodontal disease (Lindhe, 2008). The highest PLI mean was found in chronic periodontitis group, this could be related to the abnormally shaped gingival recession and the periodontal pocket formation in this group may increase the plaque accumulation.

The results of CI, this could be related to the increase in the plaque as the plaque is the causative factor of gingival inflammation. The GI in gingivitis group higher than control group. This can be explained by the fact that gingivitis represents the tissue robust defense reaction against the bacterial biofilm. The chronic periodontitis had highest GI mean, this could be related to the increase in plaque accumulation, which result in more gingival inflammation (Newman, *et al*., 2012).

About the results of BOP index, these finding indicate the effect of plaque accumulation on blood circulation and the actual pathophysiological process that happened more in inflamed periodontal tissue compared to the clinically healthy periodontal tissue .In addition, the severity of bleeding and the affluence of its incitement depend on the intensity of the inflammation. Where more accumulation of plague with increased number of active sites that accord with chronic periodontitis (Carranza, *et al*., 2009).

Concerning the results of PPD and CAL in the present study, for the gingivitis group, the inflammatory process had not yet reached the attachment apparatus (periodontal ligament and alveolar bone) in order to result in attachment destruction and formation of true periodontal pocket. Therefore, there is no alveolar bone loss and no apical migration of the junctional epithelium. In chronic periodontitis group, the suspected for such results, this could be due to increase in the bacterial invasion and the amount of plaque that triggered destruction of the sulcular, junctional epithelium and surrounding alveolar bone. (Newmam, *et al*., 2012).

Salivary Biomarkers Parameters:

Salivary Prostaglandin E2 (PGE2):

In present study, it was found that salivary PGE2 level increases with increase in periodontal destruction. The mean value of PGE2 revealed a highly significant difference (P< 0.01) as shown in table (2).These findings are consistent with (Syndergaard, *et al*., 2014; Camergo, *et al*., 2015).These observations suggest that diseased periodontal tissues produce a significant amount of PGE2 level present locally in saliva. Pro-inflammatory cytokines also play a significant role in the pathogenesis of periodontal diseases in terms of both soft and hard tissue destruction. During the beginning of an inflammatory response in the periodontal connective tissue, numerous cytokines, such as PGE2, is released from cells (Korman,*et al*., 1997). These cells are junctional epithelia, connective tissue fibroblasts, and polymorph nuclear cells (PMNs) are the main source for PGE2. Any inflamation or damage cell membran of theses cells will trigger the arachidonic acid leading to the production of PGE2 (Kumar,*et al*., 2013).Therefore, that whenever increase inflammation increase in the inflammatory cells and their products from PGE2.

Salivary Matrix Metalloprotinase-8 (MMP-8):

Our results illustrated that a highly significant difference (P< 0.01) of mean values of salivary MMP-8 levels was observed among the studies groups as illustrated in table (2). The results obtained from the present study were similar to that reported by (Ebersole, *et al*., 2015). Matrix Metalloprotinase-8 is primary collagenase in effect on both types I and III collagen and produced by neutrophils that changes the integrity of soft tissues in the periodontium (Salminen, *et al*., 2014). In gingivitis, elevated MMP-8 level as the latent, inactive preform. Through the active phase, progressing to periodontitis (Sorsa, *et al*, 2010).

Salivary Alkaline Phosphatase (ALP):

The results of our research showed the increase in the activity of alkaline phosphatase in patients with gingivitis and chronic periodontitis compared to healthy subjects, the difference was highly significant (P< 0.01) among the three groups as shown in table (2). This is a consistent with (Kumar & Sharma, 2011). The increased ALP activity in periodontal disease may be because of an increase in the inflammation and bone turnover rate. Alkaline phosphatase is produced by many cells like PMNs, fibroblasts and plaque bacteria within periodontal tissues or periodontal pocket (Al-Rawi, *et al*., 2011). When a periodontal tissue becomes diseased or its cells become damaged due to edema or destruction of a cellular membrane of these cells, this intracellular enzyme is increasingly released into the saliva where it activity can be measured (Luke, *et al*., 2015).

Correlation of Prostaglandin E2 (PGE2) Levels (pg/ml) with Clinical Periodontal Parameters:

in this study, there was a significant positive correlation (P< 0.05) anda highly significant positive correlation (P<0.01)of PGE2 level in gingivitis and chronic periodontitis groups with clinical periodontal parameters as clarified in table (3). Our results agreement with (Nakashima, *et al*., 1996; Kumar, *et al*., 2013).The presence of pathogenic bacteria being essential for the initiation of inflammation (Miller, *et al*., 2010). During the host's innate defense response to bacterial lipopolysaccharide(LPS), PMNs, and other cells release PGE2 (Ozmeric, 2004).This cytokine stimuli vasodilation and increases capillary permeability, which elicit clinical signs of redness, edema, inhibition of collagen synthesis and bone resorption (Salvi, *et al*., 2008,).Prostaglandin E2 can induce bone resorption and increase the number of osteoclasts by elevate Adenosine 3-5 monophosphate levels of osteoclasts (Dziak, 1993).

Correlation of Matrix Metalloproteinase-8 (MMP-8) Levels (ng/ml) with Clinical Periodontal Parameters:

The results of present study demonstrated a significant positive correlation (P< 0.05) and a highly significant positive correlation (P<0.01) of MMP-8 level in gingivitis and chronic periodontitis groups with clinical periodontal parameters as demonstrated in table (4). Our results consistent with (Ebersole, *et al*., 2015). The inflammation triggers an immunological response, which immediately leads to the activation of MMP-8 and to the reduction of collagen (Page & Korman, 2000). Matrix metallptinase-8 level correlated with the depth of the periodontal pocket and bleeding sites. Moreover, neutrophils that are chief cellular sources of MMP-8 are also present in an increased concentration in periodontal tissues in periodontitis patients. Additionally, proteinases are a bacterial types present in microbial plaque can activate the neutrophils to produce the MMP-8 (Sorsa, *et al*., 2004). So that the positive correlation between PLI, GI, BOP, PPD and CAL, and MMP-8 level might be caused by the potential inflammatory effect through the dental plaque.

Correlation of Alkaline Phosphatase (ALP) Levels (IU/L) and withClinical Periodontal Parameters:

In gingivitis and chronic periodontitis groups the present study revealed a significant positive correlation (P< 0.05) and a highly significant positive correlation (P<0.01)between ALP levels and clinical periodontal parameters as shown in table (5). These findings are agreement with the findings of (Kumar & Sharma, 2011). There is no hesitation that bacterial plaque is a chief cause of the initiation and maintenance of gingival inflammation in addition to pocket formation and attachment loss. There are many study revealed that bacteria within supra-gingival and sub-gingival plaque are a source of ALP production (Sanikop, *et al*., 2011). The prime source for ALP is PMNs (Kunjappu, *et al*., 2012).Therefore, there are abundant PMNs in the site of periodontal tissues inflammation and they are the main source for ALP. Alkaline phosphatase was found to be positively correlated with probing depth and clinical attachment loss because there is predominance of a neutrophil in the pocket epithelium and the pocket itself (Capple, *et al*., 1996).

Correlation among Prostaglandine E2(PGE2), Matrix Metalloprotinase-8 (MMP-8) and Alkaline Phosphatase (ALP) Levels:

Regarding the relation between PGE2 and MMP-8, our results revelead a highly significant positive correlation (P<0.01) between these two biomarkers in gingivitis and chronic periodontitis groups as shown in table (6). The bacterial products initiate a local host response in periodontium tissues that includes recruitment of inflammatory cells, then generation of prostanoides and cytokines, elaboration of lytic enzymes and activation of osteoclasts (Syndregaard, *et al*., 2014). Prostaglandin E2 encourage many of the vascular changes associated with inflammation and in precise to regulate neutrophil emigration from the circulation into the periodontium. Therefore, PGE2 will trigger osteoclast activity, MMP-8 secretion, and alveolar bone resorption in chronic periodontitis (Preshaw & Taylor, 2011).

Concerning the relation between PGE2 and ALP, in this study was a significant positive correlation (P< 0.05) between these two biomarkers in gingivitis and chronic periodontitis groups as explained in table (6). These data propose that amount of ALP and PGE2 present in saliva are produced locally by periodontal tissues in inflammation and destruction. Another possible explanation, the ALP is intracellular enzyme and the PGE2 formed from phospholipid of cell membrane, so when cell membrane distracted in periodontal disease the two mediators may be liberated at the same time.

About the relation between MMP-8 and ALP, the present study revealed a significant positive correlation ($P< 0.05$) between these two enzymes in gingivitis and chronic periodontitis groups as clarified in table (6). The description for such result may be due to these enzymes belong to the same group (markers of alveolar bone loss) (Grover, *et al*., 2014). Another possibility, the major source for these two enzymes from PMNs as mention above. Therefore, we suspect, these two enzymes increased together in recruitment of these cells in periodontal tissues inflammation and destruction.

Conclusions

1- From that, we understood that the majority of the tissue damage in periodontal diseases originates from the extreme and dysregulated production of inflammatory cytokine and destructive enzymes in response to the survival of the pathogenic bacteria in supra and sub-gingival plaque.

2- As the severity of inflammation increases, there is a significant increase in the PGE2, MMP-8 and ALP levels suggesting that there is a direct relationship between these biomarkers levels in saliva and periodontal destruction**.**

3- Since PGE2, MMP-8 and ALP levels in saliva are positively correlated with clinical periodontal parameters may be considered as a potential biochemical marker for assessment of periodontal disease activity reflecting the extent of periodontal disease and it may predict future disease progression.

4- Saliva considered a good media for assessment of such inflammatory mediators in periodontal diseases.

References

Al- Rawi, N.A; Rashad, J.M and Hussain, B. (2011). Salivary Alkaline Phosphatase and Periodontal Disease. J.MDH. 8(2):208-214.

Baser, U; Germen, M; Erdem, Y; Issever, H and Yalcin, F. (2014). Evaluation of Gingival Bleeding a Wareness by Comarision of Self-Reports and Clinical Measurments of Freshman Dental Student. European J of Dentistry. 8(3):360-365.

Camargo, G.A; Santos, M.P; Silva, N.L; Miranda, A.L and Tributino, J.L. (2015). Levels of Prostaglandin E2 (PGE2) in Gingival Crevicular Fluid from Smokers and Non- Smokers with Gingivitis and Chronic Periodontal Diseases. J of Dentistry and Oral Hygiene. 7(5):54-59.

Carinci, F; Palmieri, A; Girardi, A; Cura, F and Lauritano, D. (2015). Genetic Risk Assessment of Periodontal Disease during Dental Treatments. J. Annals of Forensic Research and Analysis. 2(1): 1011- 1013.

Carranza, F.A. (2009). Clinical Periodontology. 10th Edition. WB Sounder Company; Philadelphia.

Chapple, I.L; Socransky, S.S; Dibart, S; Glenwright, H.D and Matthews, J.B. (1996). Chemiluminescent assay of alkaline phosphatase in human gingival crevicular fluid. J. Clin Periodontology. 23:587-594.

Chrzeszczyk, D;Konopka, T and Zietek, M. (2015). Polymorphisms of Toll-Like Receptor 4 as a Risk Factor for Periodontitis: Meta-Analysis. AdvClinExp Med. 24(6): 1059–1070.

Crover, H.S; Saini, R; Bhardwaj, P and Bhardway, A. (2014). Anew Down in Modern Perio-Diagnostics: Saliva and Gingival CrevicularF. J of Dental Allied Sciences 3(2): 89-92.

Dziak, R. (1993). Biochemical and Molecular Mediators of Bone Metabolism. J. Periodontology. 64:407-415.

Ebersole, J.L; Nagarajan, R; Akers, D and Miller, C. (2015). Targeted Salivary Biomarkers for Discrimination of Periodontal Health and Disease(s).J. Frontiers in Cellular and Infection Microbiology.5 (62):1-12.

Gronbland, E.A. (1998). Concentration of Immunoglobulins in Human Whole Saliva Effect of Physiological Stimulation. J. Acta Odontol Scand. 40: 87-95.

Gupta, N; Gupta, N.D; Gupta, A; Khan, S and Bansal, N. (2015). Role of Salivary Matrix metalloproteinase-8 (MMP-8) in Chronic Periodontitis Diagnosis. J. Frontiers of Medicine. 9(1):72-76.

Gustavo, G; Nascimento; Fabio, R; Leite; Marcos, B; Correa; Bernardo, L; Horta; Marco, A; Peres; Flavio, F and Demarco. (2014). Relationship between Periodontal Disease and Obesity: The Role of Life Course Events. Brazilian Dental J. 25(2): 87-89.

Khongkhunthian, S; Kongtawelert, P; Ongchai, S; Pothacharoen, P; Sastraruji, T; Jotikasthria, D and Krisanaprakornkit, S. (2014). Comparision between Two Biochemical Markers in Evaluating Periodontal Disease Severity: A Cross-Sectional Study. J of BMC Oral Health. (2014): 14-107.

Kornman, K.S; Page, R.C and Tonetti, M.S. (1997). The Host Response to the Microbial Challenge in Periodontitis: Assembling the Players. J. Periodontology. 14:33-53.

Kumar, A.K; Reddey, N.R; Babu, P.M; Reddy, V.S and Chavan, C.V. (2013). Estimation of Prostaglandin E2 Levels in Gingival Crevicular Fluid in Periodontal Health, Disease and after Treatment. J of contempclin dent. 4(3):303-306.

Kumar, R and Sharma, G. (2011). Salivary Alkaline Phosphatase Level as Diagnostic Marker for Periodontal Disease J. International OralHealth. 3(5):80-86.

Kunjappu, J.J; Mathew, V.B; Hegde, S; Kashyap, R and Hosadurga, R. (2012). Assessment of the alkaline phosphatase level in gingival crevicular fluid, as a biomarker to evaluate the effect of scaling and root planning on chronic periodontitis: an in vivo study. J. oral maxillofacial pathology. 16(1):54-57.

Lang, N.P, Bartold, P.M and Cullinam, M. (1999). Internationa Classification Workshop. Consensus report: Chronic periodontitis. J. Annals of periodontology. 4: 53.

Leong, X.F; Ng, C.Y;Badiah, B and Das, S. (2014). Association between Hypertension and Periodontitis: Possible Mechanism. J of scientific world. 2014(2014):1-11.

Lindhe, J; Karring, T and Niklans, P.L. (2008).Clinical Periodontology and Implant Dentistry. 5thEdition. Blackwell Munksgaard, a Blackwell Puplishing Company. Oxford.

Luke, R; Khav, S.N; Igbal, P.S; Soman, R.R; Chakkarayan, J and Krishnan, V. (2015). Estimation of Specific Salivary Enzymatic Biomarkers in Individuals with Gingivitis and Chronic Periodontitis: A Clinical and Biochemical Study. J. International Oral health. 7(9):54-57.

Miller, C.S; King, C.P; Jr.; Langub, M.C; Kryscio, R.J and Thomas, M.V. (2006). Salivary Biomarkers of Existing Periodontal Disease: A Cross-Sectional Study. J. Am Dent Assoc. 137:322-329.

Mutamuliza, J; Rwema, F; Ruliza, S and Ntaganira, J. (2015). Prevalence and Associated Risk Factors of Periodontal Disease among Adults Attending Dental Department in Rwanda Military Hospital (Rwanda): A Cross sectional Study. Dental Open J. 2(4): 105-111.

Nakashima, K; Giannopoulou, C and Andersen, E. (1996). A Longitudinal Study of Various Crevicular Fluid Components as Markers of Periodontal Disease Activity. J. Clinical Periodontology. 23:832–838.

Newman, M.G.; Takei, H.H.; Klokkevold, P.R. and Carrenza, F.A. (2012). Carranza s Clinical Periodontology. 11 th Edition. Elseiver; China.

Ozomeric, N. (2004). Advances in Periodontal Disease Markers. J ClinChimActa. 343(1-2): 1-16.

Page, R.C and Kornman, K.S. (2000). The Pathogenesis of Human Periodontitis: An Introduction. J. Periodontology. 14:9-11.

Paknjad, M and Rezael, A. (2013). Salivary Biochemical Markers of Periodontitis. J. BIOCHEM. 50(2): 129-146.

Preshaw, P.M and Taylor, J. (2011). How Has Research Into Cytokine Interactions and Their Role in Driving Immune Responses Impacted Our Understanding of Periodontitis? J of Clinical Periodontology. 38(11):60–84.

Rahim, Z.H.A. (1998).Saliva in Research and Clinical Diagnosis. J. Annals Dent. Uni Malaya. 5: 11-16.

Rocha, F.R.G; Molon, R.S.D; Tonetto, M.R; Munos, S.C.S and Sampaio, J.E.C. (2013). Use of Salivary Biomarkers for Diagnosis of Periodontal Disease Activity: A Literature Review. World J. of Dentistry. 4(4): 250-255.

Salminen, A; Gursoy, U.K; Paju, S; Hyvärinen, K; Mäntylä, P and Buhlin, K. (2014). Salivary Biomarkers of Bacterial Burden, Inflammatory Response, and Tissue Destruction in Periodontitis. J.Clin.Periodontology.41:442–450.

Salvi, G.E; Lindhe, J and Lang, N.P. (2008). Examination of Patients with Periodontal Diseases. Clinical Periodontology and Implant Dentistry. 5thEdition. Munksgaard; Copenhagen.

Sanikop, S.h; Bhattacharjee, S and Patil, S.A. (2011). Comparative Analysis of Serum Alkaline Phosphatase in Smokers and Non-Smokers with Chronic Periodontitis. SRM Uni J Dent Sci. 2(4): 290-295.

Sorsa, T; Hernandez, M; Leppilahti, J; Munjal, S; Netuschil, L and Mantyla, P. (2010). Detection of Gingival Crevicular Fluid MMP-8 Levels with Different Laboratory and Chair-Side Methods. J. Oral Diseases. 16:39–45.

Sorsa, T;Tjäderhane, and Salo. (2004). Matrix Metalloproteinases in Oral Diseases. J. Oral Diseases. 10(6): 311–318.

Syndergaard, B; Al-Sabbagh, M; Kryscio, R.J; Xi, j; Ding, X; Ebersole, J.L and Miller, C.S. (2014). Salivary Biomarkers Associated with Gingivitis and Response to Therapy. J. Periodontal. 2014. 85(8): e295-e303.

Taylor, J.J. (2014). Protein Biomarkers of Periodontitis in Saliva. ISRN inflammation. 2014: 1-16.

Tenovuo, J and Lagerlof, F. (1994). Saliva. In: Textbook of clinical cardiology etd. By Thylstrup A and Fejerskov O. 2nd Edition. Munksgaard; Copenhagen. 17-43.

Access this Article in Online	
	Website: www.ijarbs.com
Quick Response Code	Subject: Pathology
DOI:10.22192/ijarbs.2016.03.09.004	

How to cite this article:
Amel O. Hassan, Saad M. Hussein, Wisam W. Sahib. (2016). Salivary Biomarkers (PGE2, MMP-8, ALP Levels) and Clinical Periodontal Parameters for Segregation of Periodontal Health and Diseases. Int. J. Adv. Res. Biol. Sci. 3(9): 27-36.