ORIGINAL ARTICLE

CONTENTS

Assessment of serum Interleukin-1β and periodontal health status in patients with different stages of periodontitis

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ABSTRACT

Aim: To assess condition of periodontal health and serum levels of interleukin-1β in periodontitis and control groups and determine relationship between serum levels of interleukin-1β and clinical periodontal parameters in periodontitis and control groups.

Materials and Methods: A sample consists of 80 male participants, ages thirty to sixty. A total of twenty people were separated into four groups: twenty people with stage I, twenty people with stage II, and twenty people with stage III periodontitis. Periodontium of control group was clinically sound, for every subject, clinical periodontal parameter were measured, such as depth of probing pocket, bleeding on probing, clinical attachment level, and plaque index. Following clinical evaluation, five milliliters of venous blood were extracted from each group. Serum samples were frozen at (-20)°C after centrifusion. Level of interleukin-1β in serum was measured using mean of enzyme-linked immune-sorbent assay (ELISA).

Results: Group with stage III periodontitis had highest serum interleukin-1 β levels, which were followed by those in stages II and I. There were notable variations between groups, with control group exhibiting lowest levels of interleukin-1 β group. An increased stage of periodontitis was indicated by a statistical analysis of clinical periodontal parameters, which showed a significant difference in mean of all clinical periodontal parameters. There were non-significant weak positive correlations of interleukin-1β with all clinical measures at all periodontitis groups, with exception of a moderately positive correlation with PLI, BOP, and CAL in stage I periodontitis group.

Conclusions: Serum interleukin-1β could be used to differentiate between periodontitis stages.

KEY WORDS: periodontitis, interleukin-1β, serum, clinical periodontal parameters

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INTRODUCTION

Chronic periodontal disease (PD) is a condition linked to pathologic events that deteriorate the tooth anchoring structures. The primary characteristics of chronic periodontal disease in its advanced stages are irreversible bone loss and the breakdown of the periodontium's connective tissue apparatus. Periodontal disease is thought to be caused by complicated interactions between immune-inflammatory response and pathogenic bacterial biofilm. Numerous genetic and environmental factors, the presence of systemic diseases, and unhealthy habits like smoking all influence this interaction. Interleukin-1β (IL-1β) is an inflammatory cytokine that is part of the host's inflammatory immune response. Given that there is a strong correlation between the development of periodontitis and IL-1β, it is thought to be a potent candidate to discriminate active from latent PD**.** The inflammatory condition known as periodontal disease destroys the tissues that support teeth [1]. It first manifests as gingivitis, a reversible inflammation of periodontal soft tissue that causes bleeding and swelling of the gingiva. Gingivitis can lead to periodontitis in susceptible and immunocompromised people, which eventually causes the periodontal and bone tissue around the teeth to be destroyed. The radiographic loss of alveolar bone, attachment loss, bleeding of gingiva, periodontal pocketing, and periodontal tissue loss are the main symptoms of periodontitis [2]. Both direct tissue damage from plaque bacterial products, such as collagen-degrading enzymes and elastase-like enzymes, and indirect damage via bacterial activation of the immune responses and host inflammatory are involved in the processes underlying this destructive process [3-4]. An essential first step in diagnosing periodontal disease is evaluating the bone structure of the periodontal tissue. Lamina dura that is undisturbed can be seen on radiographic pictures of healthy periodontal tissue (both laterally and crestally).

Furthermore, the furcation area's bone looks to be intact, and distance measuring between the crest of bone and the cementoenamel junction is roughly 2 mm (with a range of 1 to 3 mm) [5]. By comparing clinical signs with alveolar bone loss interproximally, radiographic evaluation is a crucial component of the examination to validate the diagnosis of periodontitis. These results provide insight into the prognosis, course of treatment, and estimate of disease progression or recurrence [6]. As a result, radiographic measurement of bone loss becomes essential for assessing the severity and progression of the disease, as well as for staging and grading cases of periodontitis. In the early stages of periodontitis, a comprehensive periodontal examination accompanied by a radiographic evaluation of the condition should be performed [7]. Low molecular weight signaling proteins are called cytokines. They are produced by various cells that are essential to numerous physiological processes. In the course of the immunological and inflammatory processes, cytokines control the strength and duration of the response [8]. They can have a significant impact on the start and course of diseases because of their both preventive and destructive functions [9]. Interleukin-1β (IL-1β) is recognized as a major inflammatory mediator that plays a significant role in inflammatory process and immunity in periodontitis. IL-1β which is described as a gene on chromosome 2q14, it is produced by stimulated macrophages as a pro-protein. In patients with chronic periodontitis, it was the gingival tissue's first cytokine to be identified [10]. One of the best accessible biomarkers for accurately predicting the course of periodontal disease is IL1 [11]. Prostaglandin E2, platelet-activating factor, and nitrous oxide are generated due to IL-1β, which induces inflammatory vascular changes and enhances blood circulation to regions of tissue damage or infection. Given that it is known to enhance fibroblast production of collagenase and prostaglandin E2, as well as upregulate matrix metalloproteinase, IL-1β is a powerful stimulant of bone resorption in periodontal tissues. This cytokine's activity signals neutrophil and monocyte migration into the periodontal tissue from the vasculature [12]. In dental practice, periodontal disease is diagnosed using clinical periodontal parameters. However, In addition, there are a number of issues with the clinical standards that prevent them from meeting the needs of the general public in terms of determining the current state and trajectory of the disease, as these parameters need a considerable degree of damage before they can record the disease. A quick, easy, and precise way to identify and track periodontal disease should offer crucial diagnostic information in order to enhance and accelerate treatment choices and advance the field toward personalized point-of-care diagnostics [13]. According to the research question, is it possible to distinguish between different stages of periodontitis using the serum level of interleukin-1β?

AIM

To assess condition of periodontal health and serum levels of interleukin-1β in periodontitis and control groups and determine relationship between serum levels of interleukin-1β and clinical periodontal parameters in periodontitis and control groups.

MATERIALS AND METHODS

This observational case-control study was designed to answer the research question. The study's subjects were all Iraqi patients who were receiving care from the periodontics department at the University of Kufa's teaching hospital, the College of Dentistry. Sample collection began in November 2023 and continued through January 2024. After receiving all the information completely detailing the nature and objectives of the study, before being included in the study, every patient had to sign an informed consent form. Subject details, including name, age, gender, complete medical and dental history, and prescriptions, were entered into a specially created case sheet. Following consent signing, a thorough examination of the clinical periodontal parameters (PLI, BOP, PPD, and CAL) was conducted, and 5 milliliters of blood were drawn from each participant. Out of the 260 subjects that were examined for the sample collection, only 80 subjects, ranging in age from 30 to 60, met the study's requirements.

There were four groups of subjects:

Clinically healthy control group: 20 participants with no radiological bone loss, probing pocket depths ≤3 mm, probing attachment loss <10%, and probing bleeding <10% [14]. The Twenty patients in the Stage I early/mild periodontitis group had interproximal bone loss of less than 15% or (1-2 mm) clinical attachment loss. Twenty patients in the Stage II moderate periodontitis group had interproximal bone loss involving the coronal 3rd of the root or (3–4 mm) of attachment loss. Twenty patients in the Stage III severe periodontitis group had loss of interproximal bone involving the middle 3rd of the root or (≥5 mm) clinical attachment loss (14). Additionally, periodontitis cases were localized or generalized, unstable (PPD ≤4mm with BOP or PPD>5mm with or without BOP).

INCLUSION CRITERIA

1. Individuals who have at least 20 teeth.
2. Patients who appear to be in good health overall.
3. People who haven't taken antibiotics or anti-inflammatory medications in the last three months.
4. Patients who range in age from thirty to sixty.

EXCLUSION CRITERIA

1. Individuals who have had extensive periodontal treatment as well as antimicrobial or anti-inflammatory therapy within the last 3 months.
2. Consuming alcohol or smoking.
3. Patients with chronic systemic diseases; pregnant women, those using birth control pills, and nursing mothers; immunocompromised patients.
4. Individuals suffering from disorders of the mucosa, including white and red lesions, ulcers, and hard and soft palates.
5. Patients with crowns, bridges, implants, removable dentures, and orthodontic appliances.
6. People who have xerostomia.

To establish the staging of the periodontitis cases, a clinical diagnosis was made initially. The diagnosis was then confirmed by estimating the degree of bone loss by using (a periapical radiograph-parallel technique) to the dentition's most affected tooth. To confirm the diagnosis, a radiographic image of the tooth with the highest CAL score, or the most affected tooth, was obtained. To standardize the process, parallel technique was employed with the help of film holder. The primary investigator used the same equipment (Kodak 2100, New York City, USA) and digital sensor (RVG 2500, Carestream, Georgia, USA) for every radiograph. Subsequently, the radiographs were displayed for analysis and measurement on a digital screen in (Sarona, Pennsylvania, Germany). From the CEJ to the most apical point of bone destruction visible in the radiographic image, the amount of bone loss was measured. The software used to process the radiography images had a ruler option that helped measure this distance in millimeters. Root length was divided into three thirds namely; coronal, middle, and apical. To confirm the staging of periodontitis, the radiograph's location of the current bone level was determined. A radiology specialist trained the principal investigator on the X-ray software program before the study's starting. The same radiologist also examined and verified the measurements and the degree of bone resorption in each instance. Clinical parameters, including BOP, PPD, CAL, and PLI [15], were measured for each dentition that is currently in use. A University of Michigan O probe with Williams markings at 1, 2, 3, 5, 7, 8, 9, and 10 mm was used to perform a full mouth examination at six sites per tooth (mesiobuccal, buccal, Distobuccal, mesiolingual, lingual, and distolingual). Wisdom teeth were not included in the study. Four surfaces (mesial, buccal, distal, and lingual) were examined. A five milliliter plastic disposable syringe was used to extract five milliliters of venous blood from each participant after the clinical periodontal parameters were evaluated. The sera were then separated after the blood was transferred into jell-separating tubes and centrifuged for fifteen minutes at 1000x g. Following labeling, the tubes were kept at -20°C until the Enzyme-Linked Immuno-Sorbent Assay (ELISA) was used to measure the amount of IL-1β in the serum. The AL-Mustafa laboratory in Karbala is where the laboratory tests were conducted.

PRINCIPLE OF THE ASSAY OF SERUM IL-1B

The Human (IL-1β) level in serum samples is measured using the Bioassay Technology Laboratory IL-1β ELISA kit, which employs a double-antibody sandwich enzyme-linked immunosorbent assay (ELISA). Fill the wells for Chapter Two with (IL-1β). Content and Approach the 38 monoclonal antibody enzyme is pre-coated with Human (IL1β) monoclonal antibody prior to the addition of biotin-labeled (IL-1β) antibodies and their combination with streptavidin-HRP to form an immune complex. The next step is incubation. Finally, additional washing and incubation are carried out to get rid of any unbound enzymes. The liquid turned blue when Chromogen Solutions A and B were added to the wells, and yellow when acid was added at the end. Positive correlation was observed between the concentration of Human Substance (IL1β) in the sample and color chroma.

STATISTICAL ANALYSIS

Utilizing the Statistical Package for Social Science (SPSS version 21) (Chicago, USA, Illinois), the data were described, examined, and displayed.

Two categories can be used to group statistical analyses:

1. Descriptive analysis: (minimum, maximum, mean, and standard deviation and Standard error).
2. Inferential analysis:

a) One Way -Analysis Of Variance (ANOVA): statistical test for the difference between independent groups using the Games-Howell posthoc test (Unequal variance).

b) Pearson correlation (r): parametric test for the linear correlation between two quantitative variables.

Significant (S) $P<0.05$, Not significant (NS) $P>0.05$.

RESULTS

Table 1 displays the age distribution of study participants across study groups. Age-wise, there were notable differences between the groups, but as people aged, their periodontitis stages also increased. As demonstrated in Table (2) the study's findings indicate a highly significant difference in all periodontal parameters between the periodontitis and control groups. The highest mean value of PLI (86.41) was in the Stage III,

Table 1. Statistical analysis for age parameter among all groups

Groups	Mean	±SD	±SE	Minimum age	Maximum age	F	P value
Control	37.8	1.095	0.489	30	39	70.194	0.000 S
Stage I	43.2	1.483	0.663	36	45		
Stage II	45.2	1.095	0.489	37	47		
Stage III	48.8	0.836	0.374	39	50		

Table 2. Descriptive and statistical test of parameters among groups using One Way- Analysis Of Variance (ANOVA)

Variables	Groups	Mean	±SD	F	P value
PLI	Control	53.21	9.718	1651.405	0.000 S
	Stage I	78.39	12.171		
	Stage II	83.36	9.568		
	Stage III	86.41	9.424		
BOP	Control	7.30	0.176	283.579	0.000 S
	Stage I	45.56	0.403		
	Stage II	57.77	0.45		
	Stage III	74.64	0.424		
PPD	Stage I	4.36	0.147	151.961	0.000 S
	Stage II	4.89	0.09		
	Stage III	5.58	0.082		
CAL	Stage I	1.79	0.137	297.6	0.000 S
	Stage II	2.80	0.084		
	Stage III	3.76	0.118		

Table 3. Multiple pair wise comparisons of clinical parameters between groups using Games-Howell posthoc test

Groups	Games-Howell post hoc test	PLI	BOP	PPD	CAL
Control - Stage I	Mean Difference	-25.172	-	-	-
	p-value	0.000 S			
Control - Stage II	Mean Difference	-30.150	-	-	-
	p-value	0.000 S			
Control - Stage III	Mean Difference	-33.196	-	-	-
	p-value	0.000 S			
Stage I - Stage II	Mean Difference	-4.978	-12.210	-0.528	-0.738
	p-value	0.000 S	0.000 S	0.001 S	0.000 S
Stage I - Stage III	Mean Difference	-8.024	-29.074	-1.216	-1.968
	p-value	0.000 S	0.000 S	0.000 S	0.000 S
Stage II - Stage III	Mean Difference	-3.046	-7.205	-0.688	-1.230
	p-value	0.000 S	0.4373 NS	0.000 S	0.000 S

followed by Stage II was (83.36) then Stage I was (78.39) and finally the Control group demonstrated the lowest mean value was (53.21), while the highest mean value of BOP (74.64) was in the Stage III, followed by Stage II was (57.77) then Stage I was (45.56) and the Control group demonstrated the lowest mean value was (7.30). Additionally, Stage III showed the highest mean value of "PPD" was (5.58) among the periodontitis groups followed by Stage II which was (4.89) and Stage I group was (4.36). Regarding Stage III showed the highest mean value of "CAL" was (3.76) among the periodontitis groups followed by Stage II was (2.80) and Stage I group was (1.79). Significant differences were found between Stage III and both Stage II and Stage I groups, as well as between Stage II and Stage I groups, when all clinical periodontal parameters were compared across study groups, excpet in BOP the inter group comparisons between Stage III with Stage II revealed, non-significant difference as can be noticed in (Table 3). According to the biochemical analysis table (4), the

Table 4. Descriptive and statistical test of serum IL-1β (pg\mL) among groups using One Way ANOVA

Groups	Mean	±SD	±SE	Minimum age	Maximum age	F	P value
Control	21.14	0.914	0.408	20.12	22.36	2404.239	0.000 S
Stage I	30.85	0.547	0.244	30.25	31.25		
Stage II	38.34	0.182	0.081	38.23	38.65		
Stage III	49.29	0.087	0.039	49.14	49.36		

Table 5. Multiple pair wise comparisons of serum IL-1β (pg\mL) between groups using Games-Howell posthoc test

Groups	Groups	Mean Difference	P - value	Significance
Control	Stage I	-9.7020	0.000	S
	Stage II	-17.1920	0.000	S
	Stage III	-28.1460	0.000	S
Stage I	Stage II	-7.4900	0.000	S
	Stage III	-18.4440	0.000	S
Stage II	Stage III	-10.9540	0.000	S

Table 6. Correlation of serum IL-1 β with clinical periodontal parameters in periodontitis groups

Parameters	Statistical analysis	Stage I	Stage II	Stage III
PLI	r	0.710	0.083	0.208
	p value	0.179	0.895	0.737
	Sig	NS	NS	NS
BOP	r	0.686	0.239	0.474
	p value	0.201	0.698	0.420
	Sig	NS	NS	NS
PPD	r	0.489	0.768	0.460
	p value	0.403	0.129	0.436
	Sig	NS	NS	NS
CAL	R	0.655	0.241	0.316
	p value	0.230	0.696	0.605
	Sig	NS	NS	NS

mean value of serum IL-1 β levels in Stage III was the highest of the four groups at 49.29 pg/mL, stage II had the next-highest mean value at 38.34 pg/mL, followed by stage I group 30.85 pg/mL and the Control group had the lowest mean value at 21.14 pg/mL with significant differences through the groups. The comparisons of IL-1 β levels between all pairs of the periodontitis and control groups in table (5) showed highly significant differences. In the current study, PLI, BOP, and CAL showed a moderately positive correlation with serum IL-1 β in the stage I group, indicating a relationship between these clinical periodontal parameters and IL-1 β. Overall, the relationship between periodontal parameters and serum IL-1 β was weakly positive and insignificant; in stages II and III, the relationship was also weakly positive and insignificant. These findings are shown in (Table 6).

DISCUSSION

Loss of the tissues supporting teeth is progressive and irreversible in periodontitis, a multifactorial inflammatory disease. An imbalance between the host immune response, which includes elevated levels of cytokines like IL-1β that may hasten periodontal destruction, and the microbial tooth biofilm is the cause of the disease's progression [15]. The results of this investigation demonstrated that the control and periodontitis groups had different age distributions, with the control group having the lowest mean age. These results were in line with research [16-17] that demonstrated how the amount of time periodontal tissues are exposed to bacterial plaque is likely connected with the severity of periodontal disease and bone loss that increases with age. It is also thought that these outcomes reflect a person's entire oral history. The results of the study demonstrated that the stage I group had the lowest mean PLI value and that there was a significant difference in its values as the severity of periodontitis increased. These findings agreed numerous studies [12, 18-19] that found the severe group had mean PLI values that were higher than those of the other periodontitis groups. These results may be explained by the control subjects' good oral hygiene practices, healthy periodontium, and successful plaque control [20]. Furthermore, plaque is the primary etiological factor in periodontal disease and is thought to be more common in patients with periodontitis because it builds up a biofilm on the surfaces of the teeth, which allows bacteria to invade and release toxins that further damage periodontal supporting tissue [21]. The group with stage III periodontitis had the highest mean percentage of BOP with a significant difference, according to the study's findings. These findings could be the result of histopathologic alterations that cause aberrant gingival bleeding in the presence of gingival inflammation. These

alterations include ulceration or thinning of the sulcular epithelium, as well as engorgement and dilation of the capillaries. Mild stimuli can rupture capillaries, leading to gingival bleeding due to the capillaries' closer proximity to the surface and more inflammatory, and the thinned, degenerated epithelium is less protective [16, 22]. These findings were consistent with [23-24] whose research revealed that periodontitis groups had higher bleeding sites than the control group. The study's conclusions showed that the stage I periodontitis group had the lowest PPD and CAL mean values, and their mean values increased from (Stage I to Stage III groups) with a significant difference, and these results agreed with [25]. In periodontitis, increased bacterial invasion and plaque buildup resulted in damage to the alveolar bone, breakdown of the sulcular and junctional epithelium, and other issues [26]. More recently, it was demonstrated that mechanisms leading to the destruction of collagen and bone are activated by the host's immune -inflammatory response to the initial and ongoing bacterial infection. These mechanisms involve various cytokines, some of which are typically produced by cells in non-inflamed tissue and others of which are produced by cells that are involved in inflammatory process, like monocytes, PMNs, and other cells. This leads to degradation of collagen & bone [22]. The study's findings demonstrated that the control group's mean IL-1 β value was the lowest and this value significantly increased as periodontitis progressed. Many studies have investigated the ability of IL1β to discriminate periodontitis were in harmony with this study [27-29] despite differences in details of these studies. In a study [30], IL1β has shown a potential to differentiate not only controls from periodontitis patients, but also was able to distinguish between gingivitis and periodontitis. IL1β is a potent pro-inflammatory mediator that is released during inflammation from a variety of cells. Periodontal disease is mostly triggered by inflammatory bacterial products that stimulate the cells that secrete IL1β mainly macrophages and dendritic cells. In addition, keratinocytes and fibroblast release IL1β as part of their regular function, small amounts of IL1β have also been found in healthy periodontium [31]. The most notable pathogenic event caused by excessive amounts of, IL1β during periodontitis is the induction of bone resorption. The released IL1β by the activated cells promotes fibroblast secretion of PGE2 which triggers activation and differentiation of osteoclasts; which eventually leads to bone resorption [32]. Serum IL-1β levels and clinical periodontal parameters have been found to positively correlate in all groups with periodontitis. This implies that IL-1β levels may be a sensitive and accurate indicator of tissue damage caused by chronic inflammation. It is believed that IL-1β plays a major role in the progression of periodontal disease. It is well known that IL-1β stimulates the growth of endothelial cells, keratinocytes, and fibroblasts in periodontal tissues. It also causes fibroblasts to produce more collagenase, hyaluronate, fibronectin, and prostaglandin E2. Additionally, it promotes the synthesis of MMP and inhibits the growth of tissue inhibitors of MMP, which results in attachment loss, an increase in PPD, and bone resorption [33]. Limitations of this study included the sample size for the study was small. Patients with diabetes, smoking, or periodontitis were not included in the current study as additional risk factors. Additionally, the current study did not take gingivitis and stage IV periodontitis into account. Further, the technically complex and sensitive ELISA method may result in reporting false positive and false negative results. To eliminate the chances for any technical errors, specialized laboratory tools and a skilled technician are required.

CONCLUSIONS

Individuals with stage III periodontitis have greater levels of the inflammatory marker IL-1β than other groups. Furthermore, a correlation was observed between cytokine levels and a number of clinical periodontal parameters. It may be possible to distinguish between various stages of periodontitis using serum levels of IL-1β.

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CONFLICT OF INTEREST
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