Effect of Initial Periodontal Treatment on Interleukin-1β Gingival Crevicular Fluid with Chronic Periodontitis: A Rapid Review

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Abstract

Interleukin-1β, a cytokine, has elevated levels in the gingival crevicular fluid of individuals diagnosed with chronic periodontitis, and plays a significant role in the pathogenesis of periodontal tissue deterioration. The use of initial periodontal therapy is a viable therapeutic approach aimed at mitigating the progression of subsequent periodontal deterioration. The objective of this research is to assess the impact of early periodontal therapy on the levels of Interleukin-1β in the gingival crevicular fluid of individuals diagnosed with chronic periodontitis.

This article is written using the rapid review method which uses screening and searching articles referring to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines. Article searches were conducted via PubMed, Cochrane, Sciencedirect, and Wiley. The inclusion criteria in this study were articles with randomized control trials and experimental studies on clinical and biological parameters of Interleukin-1β gingival crevicular fluid published within the last 10 years.

A total of seven articles were reviewed using clinical and biological parameters Interleukin-1β in evaluating the effect of initial periodontal treatment in chronic periodontitis patients. All articles showed a decrease in the biological parameters of Interleukin-1β after initial periodontal treatment.

This review shows that initial periodontal treatment can significantly reduce Interleukin-1β levels in the gingival crevicular fluid of chronic periodontitis patients.

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Introduction

Periodontitis is a complex pathological condition characterized by the progressive degradation of the periodontal tissue.[1,2] Based on the 2018 Riskesdas data, the prevalence of periodontitis in Indonesia reached 74.1%. Periodontitis is estimated to have a global prevalence ranging from 10.5% to 12%, making it the sixth most prevalent illness worldwide.[3,4] Chronic periodontitis is the prevailing manifestation of periodontitis, exhibiting distinctive features of a gradually progressing inflammatory condition.[5] In the year 2010, the global prevalence of chronic periodontitis was observed to impact around 10.8% or a total of 743 million individuals.[6] The causes of periodontal disease consist of local and systemic factors. Local factors such as plaque bacteria and calculus accumulation on the tooth surface are the most common cause of chronic periodontitis[5]

Chronic periodontitis is distinguished by the presence of inflammation within the periodontal tissue, the creation of pockets, and the gradual loss of attachment.[5,7] This pathological condition may lead to the degradation of periodontal tissue, tooth movement, and ultimately tooth exfoliation.[8] Clinical symptom and sign assessments alone are not enough to evaluate the disease activity status.[9] The evaluation of inflammation severity may also be conducted by the measurement and analysis of gingival crevicular fluid.[10] The gingival crevicular fluid is an inflammatory exudate that is contained cytokine in a significant amount and used as the diagnostic marker of

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periodontal destruction prognosis.[11] This fluid serves as an optimal means for identifying bacterial-host interactions and serves as an indicator of the extent or severity of periodontal inflammation.[12] Collection of gingival crevicular fluid is performed non-invasively and efficiently as a biomarker sample for inflammation and bone resorption in the oral cavity.[12]

The involvement of pro-inflammatory cytokines in the pathogenesis of periodontal tissue destruction is evident. Interleukin-1β is often seen in gingival crevicular fluid, indicating the presence of cytokines.[13] IL-1β is the major cytokine produced in inflamed tissue, released by macrophages and monocytes.[14] Extensive investigation has been conducted to examine the involvement of IL-1β in the etiology of periodontal disease. Interleukin-1 beta (IL-1β) serves as a potent inducer of bone resorption, making it a significant cytokine in the context of periodontitis.[15] These pro-inflammatory cytokines act as markers for early resorption that will directly affect the mechanism of bone resorption.[16] In many research, it has been shown that the levels of IL-1β also potentially as biomarkers of periodontitis exhibit an elevation in individuals diagnosed with chronic periodontitis.[17]

The commencement of periodontal therapy serves as the primary measure in impeding the progression of periodontal disease. The primary objective of periodontal therapy is to eliminate bacterial plaque and calculus as a local irritating factors that play role in development of the disease.[18] The initial phase of periodontal treatment can eliminate existing etiological factors.[7] The first phase of periodontal therapy include the provision of oral hygiene training, the implementation of scaling and root planing procedures, as well as the establishment of control measures. Scaling and root planing also known as a common dental procedures to treat chronic periodontal disease due to their ability to effectively mitigate inflammation and inhibit bacterial growth inside the gingival crevicular sulcus.[18]

After doing a comprehensive search across many databases, it is evident that there is a paucity of research that have substantiated the impact of early periodontal therapy on IL-1β levels. The current body of research mostly focuses on investigating the correlation between levels of IL-1β and the occurrence of chronic periodontitis. Hence, the author expresses a keen interest in doing a prompt evaluation to examine the impact of early periodontal therapy on the levels of IL-1β in the gingival crevicular fluid of individuals diagnosed with chronic periodontitis. The objective of this research is to investigate the impact of early periodontal therapy on the levels of IL-1β, with the aim of identifying suitable treatment strategies and enhancing understanding of the management of inflammation in individuals with chronic periodontitis.

Materials and methods

The research used the quick review approach to conduct the article search strategy, according to the principles outlined in the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA). The literature review inquiries were formulated using the PICO framework, which centers on the elements of Population, Intervention, Comparison, and Outcome, as delineated below: (1) The study population consists of individuals diagnosed with chronic periodontitis. (2) The intervention being investigated is the administration of initial periodontal treatment. (3) The comparison group comprises patients with chronic periodontitis who have not yet received initial periodontal treatment. (4) The primary outcome of interest is the impact of initial periodontal treatment on inflammation in the periodontal tissue, as measured by the biological parameter of IL-1β levels in the gingival crevicular fluid. The user performed article searches by using the PubMed, Cochrane, ScienceDirect, and Wiley databases. Boolean operators, such as "AND," "OR," and "NOT," were used to combine basic terms. The search terms used in the article retrieval process throughout PubMed, Cochrane, ScienceDirect, Wiley, and Google Scholar included the combination of ((((periodontitis) AND (scaling root planing)) OR (initial treatment)) AND (gingival crevicular fluid)) AND (interleukin-1).

The study's inclusion criteria included randomized control trial and experimental studies that investigated the clinical and biological characteristics of IL-1β in gingival crevicular fluid. These articles were required to be written in either English or Indonesian and had been published within the last decade. The journals included in this study were selected based on their extensive availability or accessibility in full-

text format. The study used specific exclusion criteria, which including systematic review and meta-analysis publications, studies using non-human subjects, and research done on individuals with chronic periodontitis in conjunction with other medical conditions. Data taken from each article included the researcher's name and year of publication, article title, sample size, study duration, parameters, intervention, research results, and conclusions. The data generated from the screening process using the inclusion criteria will then be analyzed based on qualitative or thematic analysis, as needed by the researcher and research objectives.

Results

The process of identifying articles using keywords in databases with an initial screening system resulted in 43 articles from PubMed, 165 articles from Cochrane, 229 articles from Wiley, and 2 articles from ScienceDirect, totaling 439 collected articles within the last 10 years. A total of 95 articles were eliminated from consideration as a result of duplication, resulting in a final sample size of 344 articles. After conducting a thorough review of the titles and abstracts, a total of 252 articles were excluded from the study due to their lack of relevance to the research issue. Consequently, the remaining dataset consisted of 92 articles that were deemed pertinent to the investigation. The subsequent phase included evaluating the eligibility of the publications, wherein 17 papers were removed due to their failure to match the predetermined inclusion criteria. Consequently, a total of seven articles were selected for inclusion in this research (Figure 1).

The impact of early periodontal therapy on chronic periodontitis patients was evaluated in the seven publications by using clinical and biological measures of Interleukin-1β. All the publications documented a significant reduction in IL-1β levels after the first periodontal therapy, which included the procedures of scaling and root planing.

Discussion

Chronic periodontitis is a persistent inflammatory reaction triggered by periodontopathic bacteria present in tooth biofilm, leading to gradual deterioration of the periodontal tissue.[1] It is hypothesized that the etiology of inflammation in periodontitis involves an upregulation in the release of Interleukin-1β (IL-1β), a key cytokine implicated in the inflammatory response and serving as the primary mediator of inflammation in periodontal disease.[7,22] IL-1β secretion has also been known to play a role in inducing bone resorption and inhibiting bone formation.[17] The buildup of interleukin-1 beta (IL-1β) initiates a cascade of inflammatory responses, contributing to the development of periodontitis. This process involves the stimulation of endothelial cells, leading to the upregulation of matrix metalloproteinase (MMP) production. Additionally, IL-1β promotes the creation and activity of osteoclasts, further exacerbating the pathological effects of periodontitis.[15,24] Elevated osteoclast activity leads to heightened alveolar bone resorption, whilst the upregulation of matrix metalloproteinases (MMPs) contributes to the breakdown of the extracellular matrix, hence inducing resorption of the periodontal ligament.[15]

Elevated concentrations of interleukin-1 beta (IL-1β) are often seen in the gingival crevicular fluid of individuals diagnosed with periodontitis.[25] The gingival crevicular fluid is an exudate with inflammatory properties that may be conveniently obtained in a clinical setting. It can be used as a valuable indication for assessing the extent of periodontal disease.[26] Most studies collect the gingival crevicular fluid using filter paper strips over a certain length of time and assess the quantity using specialized biomarker assays since it is simple and sensitive. Increased levels of IL-1 in gingival crevicular fluid have been detected in the studies listed in Table 1. Five studies measured IL-1 levels in gingival crevicular fluid using Enzyme-Linked Immunosorbent Assay, one research utilized Cytometric Bead Array, and one study used Cytokine Antibody Array.

Periodontal disease may be diagnosed, monitored, and managed with the use of IL-1 level changes.[12,27] Table 1 presents three studies that demonstrate a statistically significant disparity in IL-1β levels between individuals diagnosed with chronic periodontitis and those with a healthy periodontium. The research conducted by Görgün et al. and Toker et al. revealed that the levels of IL-1β were markedly elevated in the group with chronic

periodontitis compared to the control group with good periodontal conditions. Konopka et al. found comparable results, demonstrating that levels of IL-1β were considerably reduced in individuals with a healthy periodontium compared to those diagnosed with chronic periodontitis. Increased IL-1β was also observed in chronic periodontitis patients with periodontal damage measured by clinical parameters, including pocket depth. A total of seven studies in table 1 used clinical parameters such as pocket depth. In assessing periodontal damage, there were no restrictions or grouping, but patients with deeper pocket depths showed higher IL-1β levels, as seen in table 2.[28] Hyun et al. found that higher IL-1β levels were present in patients with deep pocket depths compared to shallow pocket depths. [23,29] This supports the idea that the cytokine IL-1β is closely related to the severity and tissue damage of periodontal disease and that pocket depth is directly proportional to the increase in IL-1β levels. [30] There are unit differences in expressing the amount of IL-1β levels, as well as differences in the method of calculating IL-1β levels, which make the measurement results in table 2 more varied.

The main treatment for chronic periodontitis is to eliminate plaque and other etiologic factors in order to stop the inflammatory process in the periodontal tissue and achieve good periodontal health.[1] The presence of bacterial endotoxins has been shown to elicit inflammatory responses and induce damage to the periodontal tissue. The use of scaling and root planing (SRP) as a first non-surgical intervention for periodontal disease has shown favorable outcomes, particularly in terms of clinical and biological indicators.[19] Studies in Table 1 concluded that clinical and biological parameters improved after SRP was performed.[22] Table 2 shows a significant reduction in IL-1β after to SRP. The study conducted by Konopka et al. revealed a statistically significant decrease in the levels of IL-1β in the gingival crevicular fluid after a period of four weeks after SRP. This reduction was accompanied by a notable improvement in the clinical parameters.[22] The study by Üstün et al. reported a significant decrease in the biological parameter IL-1β at 1 and 3 months after SRP.[19] Eltas et al. concluded that a reduction occurred at 3 months after initial periodontal treatment with SRP. Differences in control results may occur because there were interventions in the form of oral hygiene instructions that were only carried out in some studies. Based on the research in Table 2, it can be concluded that a significant decrease in IL-1β levels and improvement in clinical parameters occur in the first to second month after SRP is performed. This may occur because after the pathogens are eliminated, the infiltration of inflammatory cells is no longer widespread, the inflamed area decreases, and new epithelial attachment has fully formed after 1 month of SRP.[22]

The efficacy of mechanical therapy, namely SRP in isolation, may be limited in completely eradicating pathogenic bacteria. This is mostly owing to the bacteria's presence inside the periodontal tissues, which are inaccessible to periodontal tools, as well as the presence of lesions including furcations.[31] Several other studies have conducted research on combining initial periodontal treatment with additional treatment using lasers, which became a barrier for the author in the process of compiling this article. The additional use of lasers with mechanical treatment is considered potentially increasing the healing of chronic periodontitis because lasers have excellent ability to effectively remove plaque and calculus with strong bactericidal effects. Laser therapy has the potential to help chronic periodontitis treatment with root surface debridement, however there is currently no research that shows laser application promotes clinical progress. Therefore, further research is needed regarding the effectiveness of laser treatment for periodontal tissue damage.

Conclusions

This study shows that patients with chronic periodontitis have higher levels of IL-1β compared to patients with healthy periodontal tissues. Based on the results obtained from this review article, it can be concluded that initial periodontal treatment in the form of SRP is capable of reducing the levels of IL-1β in gingival crevicular fluid in patients with chronic periodontitis.

Declaration of Interest

The authors report no conflict of interest.

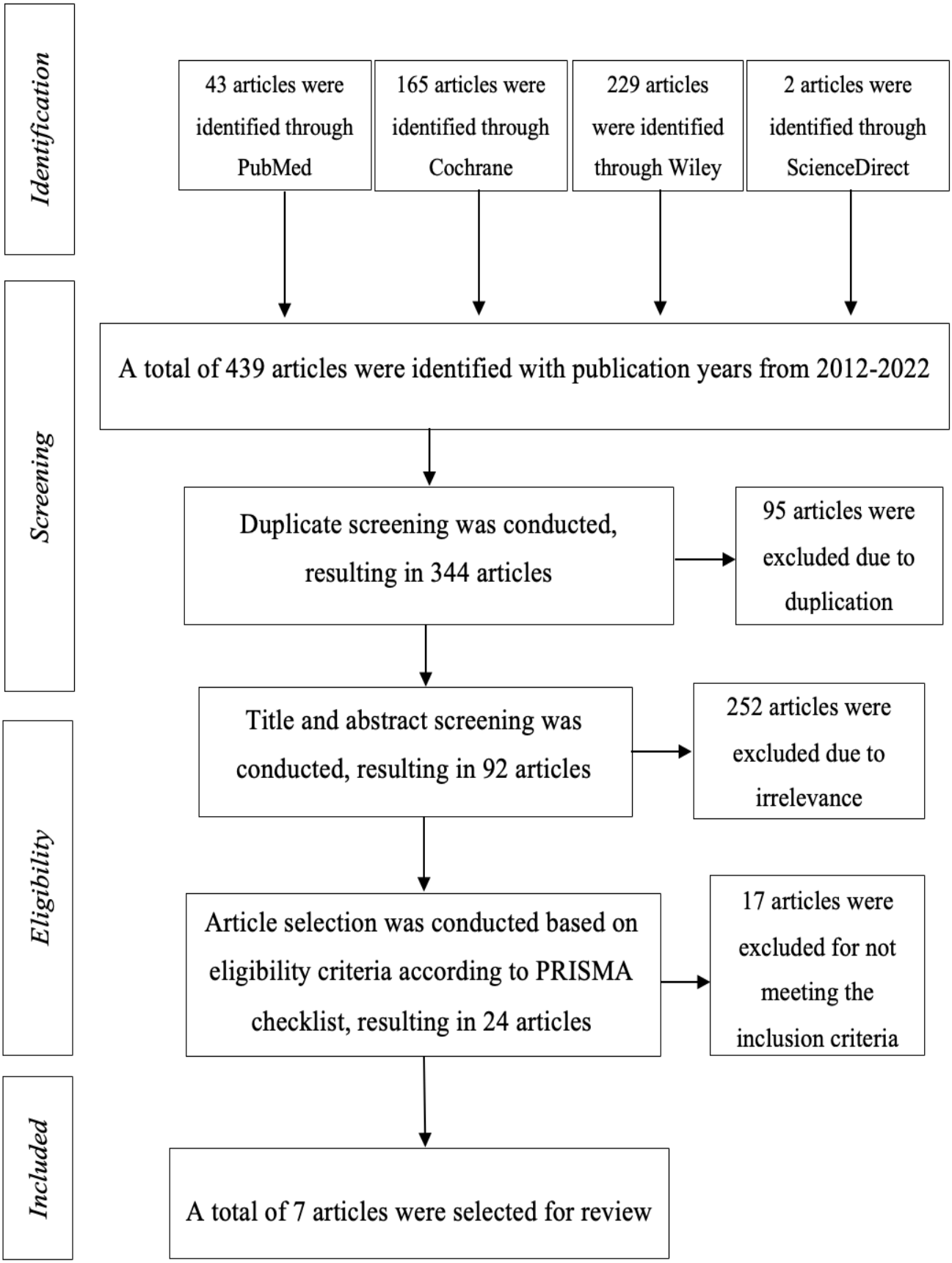

Figure 1. PRISMA flowchart.

Author, (Year of publication)	Sample Size	Study Duration	Parameters	Intervention	Results	Conclusion
Konopka et al.[19] (2012)	51 with chronic periodontitis and 21 healthy periodontal patients	Baseline, 1 week, 4 weeks	PI GI PPD CAL IL-1β IL-8	Chronic periodontitis patients were given SRP, while 21 healthy periodontal patients were not treated	Levels of IL-1β were lower in healthy periodontal than in chronic periodontitis at baseline.	SRP can significantly reduce levels of IL-1β.
Toker et al.[20] (2012)	10 healthy periodontal and 30 chronic periodontitis: 15 smokers and 15 non-smokers	Baseline, 6 weeks	PPD CAL GI PI BOP IL-1β	Non-surgical periodontal treatment consisting of oral hygiene instruction and SRP.	IL-1β levels were higher in chronic periodontitis and the highest IL-1β levels were found in chronic periodontitis who smoked before and after SRP.	Increase in IL-1β levels in chronic periodontitis and found that initial periodontal treatment was effective in reducing IL-1β levels.
Eltas et al.[21] (2012)	20 generalized chronic periodontitis	Baseline, 3 months, 9 months	PI GI PPD CAL IL-1β	Patients received oral hygiene instruction and SRP, the test side received SRP + NDL treatment, and the control side only received SRP.	IL-1β levels were lower in the test side receiving SRP + NDL compared to the control side receiving only SRP, but the difference was not significant.	SRP + NDL treatment in periodontal pockets was more effective than SRP only in reducing IL-1β.
Üstün et al.[7] (2014)	21 chronic periodontitis.	Baseline 1 month, 3 months, 6 months	PPD GI PI CAL IL-1β	Test sites received SRP and laser treatment, while control sites received SRP only.	In the first, second, and third months, PPD and IL-1β levels were significantly lower in the SRP and laser group compared to the SRP group.	The use of diode laser as an addition to SRP improved significant clinical parameters and IL-1β levels.
Hieda et al.[22] (2017)	20 localized chronic periodontitis.	Baseline, 1 week, 2 months, 3 months	PPD BOP GCF	All patients received oral hygiene instructions and SRP.	The changes in PPD decreased significantly after SRP and a significant reduction were observed in the levels of IL-1β after SRP.	SRP resulted in improvements in clinical parameters and the healing process was affected by the decrease in the ratio of IL-1β post-SRP.
Görgün et al.[23] (2021)	35 aggressive periodontitis, 30 chronic periodontitis, and 30 healthy periodontal as a control.	Baseline, 6 weeks	GI PI CAL PPD IL-37 IL-1β	All periodontitis patients received oral hygiene instructions and SRP.	The level of IL-1β was higher in the chronic periodontitis at baseline and after initial periodontal treatment IL-1β level higher in the aggressive and chronic periodontitis than in the healthy periodontal.	Levels IL-1β increased in aggressive and chronic periodontitis and decreased after initial periodontal treatment.

Table 1. Data Extraction.

**BOP (Bleeding on Probing); CAL (Clinical Attachment Level); GI (Gingival Index); PPD (Periodontal Pocket Depth); PI (Plaque Index); GCF (Gingival Crevicular Fluid); SRP (Scaling Root Planing); IL-1β (Interleukin-1β).*

Author (Year of publication)	Pocket Depth (mm)	IL-1β Levels									Description
		Baseline	1 weeks	1 months	6 weeks	2 months	3 months	4 months	6 months	9 months	
Konopka et al.[19] (2012)	1.5±0.9	15.5± 14.0	-	-	-	-	-	-	-	-	Mean ± SD IL-1β pg/sample
	6.4±0.6	72.5±37.0	57.2±26.0	34.1±13.9	-	-	-	-	-	-	
Toker et al.[20] (2012)	4.8±0.3	438.1±294.8	-	-	377.8±296.1	-	-	-	-	-	Mean ± SD IL-1β pg/site
	1.4 ±0.5	299.4±142.7	-	-	-	-	-	-	-	-	
Eltas et al.[21] (2012)	4.04±1.23	10.2±3.60	-	-	-	-	7.79±2.17	-	-	7.28±3.73	Mean ± SD IL-1β pg/sample
Üstün et al.[7] (2014)	4.25±0.41	117.67±131.83	-	40.41±35.83	-	-	30.06±34.42	-	28.07±31.23	-	Mean ± SD IL-1β pg/30s
	5.38±0.14	5.48±1.07	-	-	-	1.15±0.13	-	0.96±0.10	-	-	
	5.4±1.2	298.09±86.93	-	-	139.40±53.64	-	-	-	-	-	
Görgün et al.[23] (2021)	5.6±1.2	152.0±96.72	-	-	137.68±73.04	-	-	-	-	-	Mean ± SD IL-1β pg/30s
	2.8±0.3	92.81±20.63	-	-	-	-	-	-	-	-	

Table 2. Pocket Depth and Interleukin-1β Levels.

**BOP (Bleeding on Probing); CAL (Clinical Attachment Level); GI (Gingival Index); PPD (Periodontal Pocket Depth); PI (Plaque Index); GCF (Gingival Crevicular Fluid); SRP (Scaling Root Planing); IL-1β (Interleukin-1β)*

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