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Original Article

Significance of IL-8 and HMGB1 expression in peripheral blood and gingival sulcus fluid of patients with chronic periodontitis

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Abstract: Objective: To quantify interleukin 8 (IL-8) and high mobility group box 1 (HMGB1) levels in the serum and gingival crevicular fluid (GCF) of patients with chronic periodontitis, and to evaluate their clinical use as serum biomarkers for disease diagnosis. Methods: A total of 92 patients with chronic periodontitis and 71 healthy controls were recruited from Department of Stomatology at Pearl River Hospital between August 2020 and August 2021. Clinical data, including plaque index (PLI), pocket probing depth (PD), clinical attachment loss (CAL), gingival sulcus bleeding index (SBI), and calculus index (CI), were recorded for all participants. Serum and GCF levels of IL-8 and HMGB1 were quantified using enzyme-linked immunosorbent assay (ELISA). Results: No significant intergroup differences were observed in age or sex distribution (P>0.05). The periodontitis group showed significantly higher GI, PD, PLI, SBI, CAL, and tooth mobility scores compared to the healthy control group (P<0.05). These indices increased progressively with disease severity (P<0.05). Conclusion: IL-8 and HMGB1 levels in the serum and GCF of patients with chronic periodontitis are positively correlated with periodontal inflammation. Combined measurement of serum IL-8 and HMGB1 may serve as an approach for the diagnosis and monitoring of chronic periodontitis.

Keywords: Chronic periodontitis, IL-8, HMGB1, periodontal indicators, gingival sulcus fluid

Introduction

Chronic periodontitis is a chronic infectious disease resulting from dysbiosis of the dental plaque microbiome and is characterized by progressive destruction of the periodontal supporting tissues [1, 2]. It has a high global prevalence and seriously affects mastication, aesthetics, and even overall health. It is closely related to systemic diseases such as cardiovascular disease and diabetes, representing a significant public health concern [3, 4]. The disease has an insidious onset and is often painless in the early stages; therefore, patients often ignore it untilirreversible damage occurs, such as tooth mobility, displacement, or even tooth loss, missing the optimal treatment window [5]. Traditional diagnostic methods mainly rely on probing depth (PD), clinical attachment loss (CAL), and radiographic evaluation of alveolar bone resorption. However, these indicators reflect only the cumulative effects of previous tissue destruction and are limited for assessing current disease activity and predicting future progression [6]. Therefore, the identification of sensitive and specific biomarkers that accurately reflect the present inflammatory status and predict disease progression is crucial for early diagnosis, individualized risk assessment, and precision management of chronic periodontitis.

The onset and progression of periodontitis results from a complex interaction between periodontal pathogens (e.g., *Porphyromonas gingivalis*) and the host immune system. Its core pathologic mechanism involves an aberrant or excessive host immune-inflammatory response to bacterial components, such as lipopolysaccharide (LPS) [7]. While the host

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immune system aims to eliminate pathogens through innate and adaptive pathways, persistent dysregulated inflammation promotes the release of abundant inflammatory mediators and proteolytic enzymes, ultimately leading to irreversible tissue damage, such as collagen fiber degradation and alveolar bone resorption [8]. Within this complex regulatory network, a variety of cytokines, chemokines, and inflammatory proteins play crucial roles.

Interleukin-8 (IL-8/CXCL8), an important member of the CXC chemokine family, is one of the most potent chemoattractants and activators of neutrophils [9]. In periodontitis lesions, gingival epithelial cells, fibroblasts, and immune cells secrete large amounts of IL-8 in response to LPS and other bacterial stimuli, establishing a high concentration gradient within the gingival crevicular fluid (GCF), which powerfully recruits circulating neutrophils to migrate across the junctional epithelium into the periodontal pocket. This forms the first line of defense against bacterial invasion [10]. However, excessive infiltration and activation of neutrophils, accompanied by degranulation and the release of reactive oxygen species (ROS) and matrix metalloproteinases (MMPs), contribute substantially to periodontal tissue destruction [11]. Elevated IL-8 levels in GCF and saliva have been consistently observed in patients with periodontitis and are positively correlated with clinical measures such as PD and CAL [12, 13]. More importantly, after effective periodontal therapy, IL-8 concentrations decline significantly as inflammation subsides, suggesting that IL-8 serves not only as a biomarker of local inflammatory burden but also as a dynamic indicator of therapeutic response. Nevertheless, further research is needed to determine the changes in its expression in peripheral blood and its consistency with local concentrations.

High mobility group box 1 (HMGB1), a nuclear protein expressed in most cells, is released extracellularly upon cellular injury or necrosis, where it acts as a potent pro-inflammatory mediator. Clinical investigations have shown that HMGB1 levels are significantly elevated in both gingival tissues and sulcular fluid of periodontitis patients and positively correlate with plaque index [20-22]. In inflamed gingiva, epithelial cells stimulated by bacterial endotoxins release HMGB1, which binds to multiple receptors to amplify the inflammatory cascade. For instance, HMGB1 can engage the receptor for advanced glycation end products (RAGE) on gingival epithelial cells and cooperate with IL-1β through Toll-like receptors 2 and 4 to activate NF-κB signaling, thereby promoting macrophage polarization and sustaining inflammation [23, 24].

Taken together, IL-8 and HMGB1 appear to participate in the pathogenesis of periodontitis and hold promise as adjunctive biomarkers for early clinical assessment. In this study, we quantified IL-8 and HMGB1 levels in both serum and GCF of patients with chronic periodontitis and further analyzed their relationship to disease progression. This may provide reference data for early diagnosis.

Materials and methods

Main reagents

Serum and gingival crevicular fluid samples were detected using commercial enzyme-linked immunosorbent assay (ELISA) kits for IL-8 (E-EL-H6008) and HMGB1 (E-EL-H1554c), both purchased from Wuhan Elabscience Biotechnology Co., Ltd.

Methods

Study population: A total of 163 individuals who attended the Department of Stomatology at Zhujiang Hospital between August 2021 and August 2022 were recruited for this study. Among them, 71 participants with clinically healthy oral conditions served as the control group (34 males and 37 females; mean age: 37.93±3.18 years). The remaining 92 participants were diagnosed with chronic periodontitis (45 males and 47 females; mean age: 38.53±3.80 years). According to disease severity, the periodontitis group was further stratified into mild (n=40), moderate (n=33), and severe (n=19) subgroups.

The retrospective protocol was reviewed and approved by the Medical Ethics Committee of Zhujiang Hospital, Southern Medical University. Written informed consent was obtained from all participants after they had been fully informed of the study procedures.

Inclusion Criteria: (1) Age ≥30 years. (2) A diagnosis of chronic periodontitis based on the criteria established by Armitage et al.: mean

CAL>2.5 mm, CAL>5 mm in at least one adjacent site across three or more quadrants, PD>6 mm in at least one adjacent site across three or more quadrants, no more than 14 missing teeth, excluding third molars, and absence of orthodontic treatment, extraction of third molars, severe caries, or congenital tooth loss. (3) Horizontal alveolar bone resorption confirmed by X-ray examination. (4) Deprivation from food or drink for two hours prior to the examination. (5) Absence of systemic diseases other than chronic periodontitis.

Exclusion Criteria: (1) Patients with obvious malocclusion, defective or overhanging restorations, or other local irritants. (2) Pregnancy or lactation. (3) Long-term antibiotic use. (4) Receipt of periodontal treatment within the six months prior to study enrollment. (5) Long-term smoking history. (6) Diagnosis of diabetes mellitus, cardiovascular disease, rheumatism, hepatic or renal dysfunction, or other systemic illnesses. (7) Poor compliance with study instructions or unwillingness to cooperate with the study protocol.

Diagnostic criteria: (1) Healthy Gingiva: Gingival index (G1) =0, with periodontal PD<3 mm throughout the dentition. No noticeable attachment loss, alveolar bone resorption, or gingival recession is observed. (2) Mild Chronic Periodontitis: Characterized by gingival inflammation and bleeding upon probing, with PD≤4 mm and attachment loss of 1-2 mm. Radiographic examination shows horizontal alveolar bone loss not exceeding one-third of the root length. (3) Moderate Chronic Periodontitis: Defined by PD<6 mm and attachment loss of 3-4 mm. Slight tooth mobility may be present, particularly in multi-rooted teeth with incipient furcation involvement. Symptoms often include gingival inflammation, bleeding upon probing, and, in more severe cases, pus production. Radiographically, horizontal or angular bone resorption extends beyond one-third but less than two-thirds of the root length. (4) Severe Chronic Periodontitis: Characterized by PD≥6 mm and an attachment loss of ≥5 mm. Marked inflammation, frequent gingival bleeding, and periodontal abscess formation may occur, often accompanied by significant tooth mobility and furcation involvement. X-ray imaging reveals alveolar bone resorption exceeding one-half of the root length, and in some instances, reaching up to two-thirds of the root length.

Periodontal indicator testing: The following periodontal clinical indicators were recorded for both the control group and the chronic periodontitis group: plaque index (PLI), probing pocket depth (PD), clinical attachment loss (CAL), gingival sulcus bleeding index (SBI), and calculus index (CI).

Sample collection: Serum sample collection: Peripheral venous blood was collected from each participant. After standing at room temperature, the samples were centrifuged at 3000 rpm for 20 minutes. The resulting supernatant was separated and stored at 4°C until further analysis.

GCF collection method: The tooth surface was gently dried with a sterile cotton ball, and the affected tooth with the greatest PD was selected for sampling. A strip of Whatman 3M filter paper was inserted into the buccal aspect of the periodontal pocket (approximately 1 mm) and removed after 60 seconds. After 3 minutes, the procedure was repeated at the same site. The two filter papers were then placed into a pre-weighed centrifuge tube, and the weighed difference was used to determine the GCF volume. The samples was centrifuged at 1000 r/min for 10 minutes at 4°C. After centrifugation, the supernatant was stored at -80°C until use. In the control group, GCF was obtained from molars and cryopreserved in the same manner.

Determination of IL-8 and HMGB1 levels: The levels of IL-8 and HMGB1 in serum and GCF samples were detected using ELISA kits according to the manufacturer's protocols.

Treatment: All patients received non-surgical periodontal therapy, which included ultrasonic supragingival scaling and subgingival scraping. Periodontal pockets were subsequently irrigated with a mixture of hydrogen peroxide and sterile saline, followed by the application of iodized glycerin. One month after treatment, serum and GCF samples were re-collected to assess IL-8 and HMGB1 levels.

Statistical analysis

All statistical analyses were performed using SPSS version 25.0, and figures were generated using GraphPad Prism version 8.0. Counted data were expressed as frequency and percent-

Table 1. Comparison of baseline clinical data between control and periodontitis groups

	Control group (n=71)	Chronic periodontitis group (n=92)	t/χ^2 value	*P*
Sex (male/female)	34/37	45/47	0.017	0.897
Age (years)	37.93±3.18	38.53±3.80	1.102	0.272

Table 2. Comparison of periodontal measurements among groups

	Control (n=71)	Mild periodontitis (n=40)	Moderate periodontitis (n=33)	Severe periodontitis (n=19)	*P*
PD	2.34±1.09	3.07±1.04*	4.40±1.24$^{*,\#}$	5.44±1.38$^{*,\#,\$}$	<0.0001
PLI	0.64±0.44	0.98±0.58*	1.55±0.56$^{*,\#}$	1.53±0.70$^{*,\#,\$}$	<0.0001
SBI	0.39±0.49	0.70±0.61*	1.70±0.73$^{*,\#}$	2.21±0.71$^{*,\#,\$}$	<0.0001
GI	0.81±0.33	1.27±0.31*	1.75±0.33$^{*,\#}$	1.92±0.41$^{*,\#,\$}$	<0.0001
CAL	0.83±0.54	2.01±0.65*	3.13±1.03$^{*,\#}$	3.99±1.35$^{*,\#,\$}$	<0.0001
Tooth mobility	0.07±0.26	1.38±0.54*	2.09±0.52$^{*,\#}$	2.53±0.70$^{*,\#,\$}$	<0.0001

Notes: GI: Gingival index, PD: periodontal probe depth, PLI: plaque index, SBI: gingival sulcus bleeding index, CAL: loss of attachment. Data are presented as mean ± standard deviation. *P<0.05, compared to the control group; $^{\#}$P<0.05, compared to the mild group; $^{\$}$P<0.05, compared to the moderate group.

age, and comparisons were performed using the chi-square (χ^2) test. Continuous variables were presented as mean ± standard deviation (SD), and intergroup comparisons were conducted using the independent samples t-test. For data with multiple groups, one-way or two-way analysis of variance (ANOVA) was performed. Ranked or ordinal data were analyzed using the rank-sum test. Correlations between serum and gingival crevicular fluid IL-8 and HMGB1 levels and periodontal characteristics were assessed using Spearman's correlation analysis. Hazard ratios (HR) with 95% confidence intervals (CI) were calculated using multivariate Cox regression analysis. *P<0.05; **P<0.01; ***P<0.001; and ****P<0.0001 were considered significant.

Results

Comparison of baseline clinical data between groups

No significant differences were observed between the chronic periodontitis group and the control group in terms of gender or age distribution (P>0.05), as shown in **Table 1**.

Comparison of periodontal indicators among groups

Compared to the control group, patients with chronic periodontitis exhibited significantly higher values of PD, PLI, SBI, CI, and CAL (P<0.05), as shown in **Table 2**.

Comparison of serum levels of IL-8 and HMGB1 between groups

Patients with chronic periodontitis exhibited markedly higher serum levels of both IL-8 and HMGB1 compared to healthy controls (P<0.05). Furthermore, serum IL-8 and HMGB1 concentrations increased progressively with disease severity, showing significant intergroup differences among the mild, moderate, and severe periodontitis subgroups (P<0.05). These results indicate that serum IL-8 and HMGB1 levels are significantly elevated in chronic periodontitis and are positively correlated with disease severity. Detailed results are presented in **Table 3** and **Figure 1**.

Comparison of GCF levels of IL-8 and HMGB1 among groups

Compared to the control group, patients with chronic periodontitis showed markedly elevated concentrations of both cytokines (P<0.05). Within the periodontitis group, IL-8 and HMGB1 levels rose stepwise from mild to severe disease, with significant differences among all three subgroups (P<0.05). These findings indicate that IL-8 and HMGB1 levels in GCF rise in parallel with disease progression and may serve as potential biomarkers for periodontal

Table 3. Comparison of serum levels of IL-8 and HMGB1 among groups

	Control (n=71)	Mild periodontitis (n=40)	Moderate periodontitis (n=33)	Severe periodontitis (n=19)	*P*-value
IL-8 (μg/L)	5.48±0.74	10.66±4.42*	14.76±7.14*,#	18.14±6.79*,#,$	<0.0001
HMGB1 (μg/L)	0.67±0.18	7.11±3.06*	9.20±3.18*,$	12.78±5.43*,#,$	<0.0001

Notes: IL-8: interleukin-8, HMGB1: high mobility group box 1. *P<0.05, compared to the control group; #P<0.05, compared to the mild group; $$P$<0.05, compared to the moderate group.

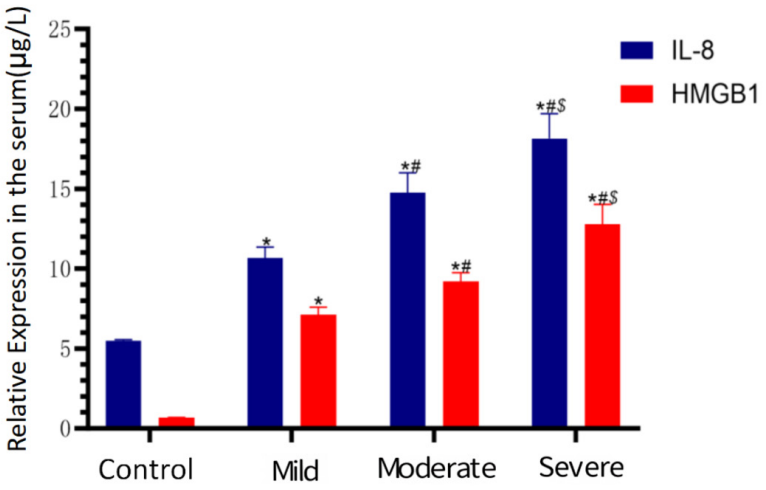

Figure 1. Comparison of serum levels of IL-8 and HMGB1 among groups. Note: *P<0.05, compared to the control group; #P<0.05, compared to the mild group; $$P$<0.05, compared to the moderate group.

inflammatory activity. Detailed results are presented in **Table 4** and **Figure 2**.

Changes in IL-8 and HMGB1 levels before and after treatment

Both serum and GCF levels of IL-8 and HMGB1 decreased significantly after therapy in patients with chronic periodontitis (P<0.05). These reductions reflect attenuation of systemic and local inflammation, and may indicate recovery of periodontal tissue integrity. Results are summarized in **Table 5** and **Figure 3**.

Correlation analysis of IL-8 and HMGB1 levels in serum and GCF

Previous studies have demonstrated a correlation between chronic periodontitis and elevated IL-8 and HMGB1 concentrations in both serum and GCF. However, the direct correlation between their systemic and local levels has not been fully clarified.

Further analysis revealed a positive correlation between serum and GCF IL-8 concentration (r=0.390, P<0.05) as well as between serum and GCF HMGB1 concentration (r=0.408, P<0.05). Results are presented in **Table 6** and **Figures 4**, **5**.

Correlations of serum and GCF levels of IL-8 and HMGB1 with periodontal measurements

Elevated IL-8 and HMGB1 levels in both serum and GCF sampled were positively correlated with periodontal PD, PLI, SBI, GI, CAL, and tooth mobility (all P<0.05). These results suggest that serum and GCF IL-8 and HMGB1 levels may serve as predictors of the severity of gingival damage in patients with chronic periodontitis. Results are shown in **Tables 7**, **8**.

Multivariate logistic regression analysis of the effects of IL8 and HGMB1 on chronic periodontitis severity

Multiple logistic regression analysis showed that age and gender were not significant predictors of the severity of chronic periodontitis. Periodontal clinical indicators such as PD, PLI, SBI, GI, CAL, and tooth mobility, as well as serum IL-8 and HMGB1 levels, were significantly correlated with the severity of chronic periodontitis (**Figure 6**).

Discussion

Chronic periodontitis is characterized by chronic, progressive destruction of the periodontal supporting tissues caused by bacterial infection. It not only exerts a profound impact on oral health but also serves as a risk factor for cardiovascular diseases, diabetes, and respiratory diseases [25-29]. Therefore, early diagno-

Table 4. Comparison of GCF levels of IL-8 and HMGB1 among groups

	Control group (n=71)	Mild periodontitis (n=40)	Moderate periodontitis (n=33)	Severe periodontitis (n=19)	*P*-value
IL-8 (μg/L)	6.16±1.11	11.81±2.96*	15.46±6.30*,#	18.36±8.31*,#,$	<0.0001
HMGB (μg/L)	2.30±2.12	6.50±3.17*	10.17±4.75*,#	16.48±5.58*,#,$	<0.0001

Notes: IL-8: interleukin-8, HMGB1: high mobility group box 1. *P<0.05, compared to the control group; #P<0.05, compared to the mild group; $$P$<0.05, compared to the moderate group.

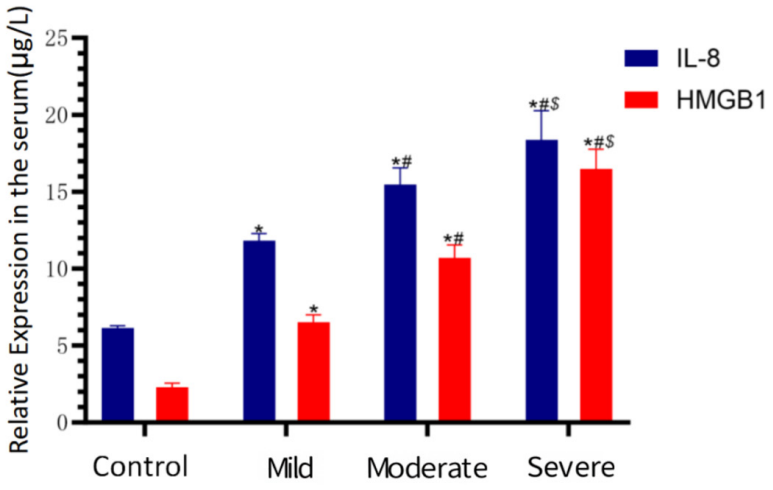

Figure 2. Comparison of IL-8 and HMGB1 levels in gingival sulcus fluid among patients with different disease severity. Note: *P<0.05, compared to the control group; #P<0.05, compared to the slight mild group; $$P$<0.05, compared to the moderate group.

sis of periodontitis is essential, as it benefits both periodontal management and the prevention and treatment of systemic disease. Currently, the diagnosis of periodontitis is primarily based on clinical periodontal examination and imaging techniques. However, these methods have certain limitations in terms of sensitivity and specificity [30, 31]. The identification of specific biomarkers is thus critical for early screening, diagnosis, and evaluation of periodontitis. During disease progression, a wide range of inflammatory mediators accumulate in gingival tissues and GCF, reflecting the inflammatory status of periodontal tissues and serving as biomarkers for disease activity [32]. GCF originates from gingival connective tissue, serum, and bacterial metabolites that infiltrate the gingival sulcus [33, 34]. It contains inflammatory cells, and its volume correlates positively with the degree of local inflammation, making it is a reliable clinical specimen for assessing inflammatory cytokine levels [35-37]. Nevertheless, GCF analysis has inherent limitations. Its collection and measurement are easily affected by the transient inflammatory state, and variations in sampling, storage, and analytical protocols across studies may lead to inconsistent biomarker quantification [38]. In contrast, serum samples offer standardized procedures for collection, storage, and analysis, are less affected by local inflammation, and provide higher diagnostic reliability. In addition, as the most commonly used biological sample in clinical practice, serum possesses broad applicability and considerable potential for the early detection of individuals at risk of developing periodontitis [39-43].

In the early stages of chronic periodontitis, the host immune defense plays a key role in resisting the invasion of periodontal pathogens [44]. Bacterial invasion activates macrophages, leading to the release of inflammatory mediators such as tumor necrosis factor-α (TNF-α), which disrupts the stability of the oral microenvironment [45]. IL-8, as a key chemokine, is one of the most potent activators and chemoattractants of neutrophils, playing a crucial role in the development and progression of periodontitis [46]. Bacterial infection enhances local inflammation and regulates IL-8 expression, thereby promoting neutrophils recruitment to lesion site. While exacerbating tissue damage and further increasing IL-8 levels. In this study, the levels of IL-8 in both GCF and serum were significantly elevated in patients with chronic periodontitis compared to healthy controls and decreased markedly after basic treatment, indicating a close relationship with the periodontal inflammatory state. Although GCF IL-8 directly reflects local inflammation, its collection and storage are susceptible to variability. In contrast, serum sampling is standard-

Table 5. Comparative analysis of IL-8 and HMGB1 levels in blood and gingival sulcus fluid before and after treatment in each group of subjects

	Mild periodontitis		*P*-value	Moderate periodontitis		*P*-value	Severe periodontitis		*P*-value
	Pre-treatment	Post-treatment		Pre-treatment	Post-treatment		Pre-treatment	Post-treatment	
Serum IL-8	10.66±4.42	6.59±2.78*	<0.0001	14.76±7.14	8.00±4.53*	<0.0001	18.14±6.79	10.68±4.07*	<0.0001
GCF IL-8	11.81±2.96	7.08±3.12*	<0.0001	15.46±6.30	8.67±4.02*	<0.0001	18.36±8.31	11.02±5.86*	0.004
Serum HMGB1	7.11±3.06	5.27±2.15*	0.022	9.20±3.18	7.39±3.87*	0.042	14.05±5.20	9.83±3.62*	0.009
GCF HMGB1	6.50±3.17	4.96±2.99*	0.045	10.17±4.75	8.24±3.84*	0.016	16.48±5.58	10.83±4.77*	0.006

Notes: IL-8: interleukin-8, HMGB1: high mobility group box 1. *P<0.05, compared to pre-treatment level.

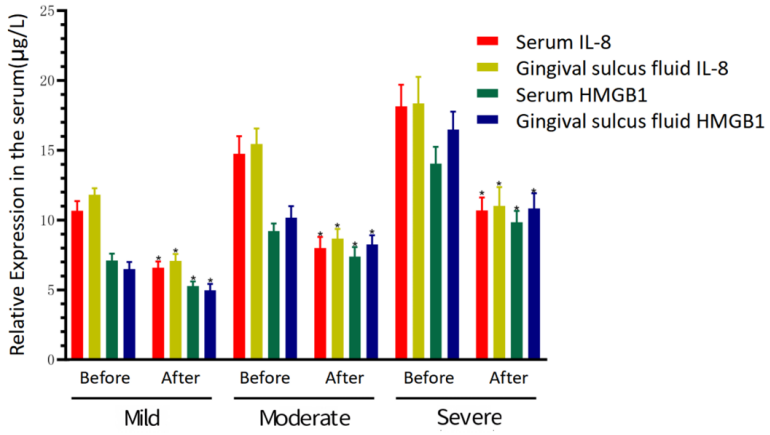

Figure 3. Comparison of IL-8 and HMGB1 levels before and after treatment in patients with different disease severity. Note: *P<0.05, compared to pre-treatment level.

Table 6. Correlation analysis between serum IL-8 and HMGB1 levels versus GCF IL-8 and HMGB1 levels

Level	Gingival sulcus fluid IL-8		Gingival sulcus liquid HMGB1	
	r	*P*	*r*	*P*
Serum IL-8	0.390	0.005	-	-
Serum HMGB1	-	-	0.408	0.000

Notes: IL-8: interleukin-8, HMGB1: high mobility group box 1.

ized and more suitable for clinical application. In this study, a significant positive correlation was observed between serum and GCF IL-8 levels. Serum IL-8 levels in patients with chronic periodontitis were approximately 24-fold higher than those in the control group, suggesting that serum IL-8 may serve as a reliable biomarker for evaluating periodontal inflammation. Owing to its high sensitivity, serum IL-8 measurement could facilitate early identification of inflammatory changes and has potential value in the diagnosis, treatment monitoring, and prognosis evaluation in chronic periodontitis.

In patients with chronic periodontitis, in addition to IL-8, the inflammatory factor HMGB1 is also highly expressed in the gingival tissue and the GCF. HMGB1 is released from the cell nucleus after local tissue damage, which can induce macrophages to secrete proinflammatory factors, thereby participating in the pathogenesis of various inflammatory diseases such as periodontitis [21]. This process forms a positive feedback loop in which persistent inflammation promotes HMGB1 secretion and accumulation within tissues. Studies have shown that HMGB1 can activate the NF-κB signaling pathway and mediate inflammation through Toll-like receptor 4 (TLR4) signaling, thereby amplifying the host immune response [47]. In this study, HMGB1 levels in both GCF and serum were significantly elevated in patients with chronic periodontitis compared to healthy controls and declined after basic periodontal treatment, suggesting a close association between HMGB1 and disease progression. In addition, a positive correlation exists between serum and GCF HMGB1 levels, suggesting that serum HMGB1 may also serve as an auxiliary indicator for assessing disease severity and monitoring treatment response in chronic periodontitis.

According to a literature review, the diagnostic sensitivity of imaging for chronic periodontitis depends mainly on the quality of the image.

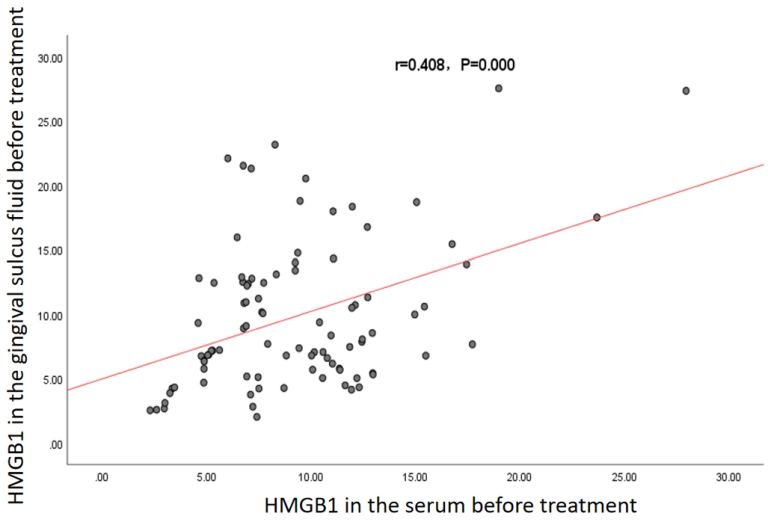

Figure 4. Correlation analysis between serum HMGB1 and GCF HMGB1 in patients with chronic periodontitis. Notes: GCF: gingival crevicular fluid, IL-8: interleukin-8, HMGB1: high mobility group box 1.

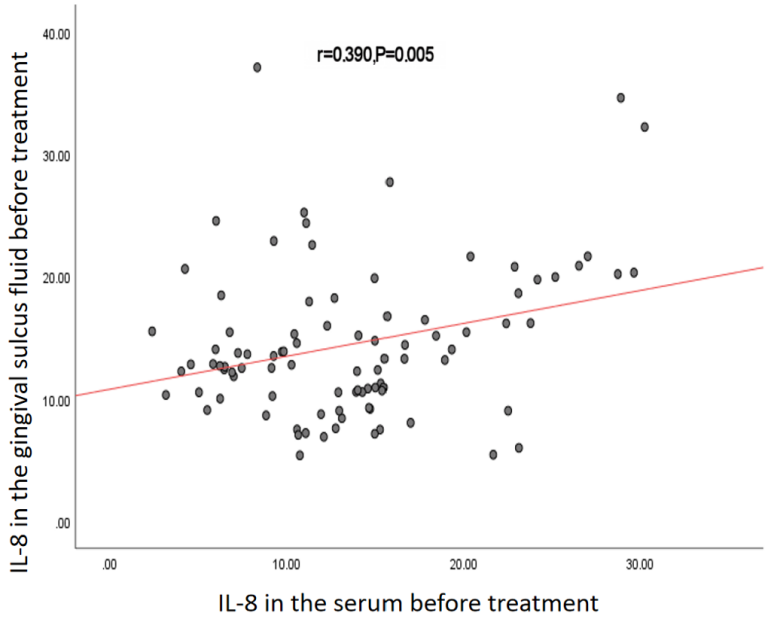

Figure 5. Correlation analysis between serum IL-8 and GCF IL-8 in patients with chronic periodontitis. Note: GCF: gingival crevicular fluid, IL-8: interleukin-8, HMGB1: high mobility group box 1.

The diagnostic specificity of high-quality X-rays is approximately 65.3%, while that of low-quality films drops to 54.9%. Although imaging techniques generally show high sensitivity, their performance varies considerably depending on the diagnostic criteria employed. For example, the sensitivity based on the EFP/AAP 2018 classification system is reported to be as high as 99.6%, whereas it drops to 87.0% under the CDC/AAP 2012 criteria [30]. In addition to variations in diagnostic standards, inter-observer interpretation bias may also contribute to discrepancies in imaging-based assessment.

In contrast, detection of IL-8 and HMGB1 are simple, reliable, and less susceptible to subjective factors. Compared with imaging examinations, serum testing, as a routine clinical test sample, has shown significant advantages in the early screening individuals at risk for periodontitis [40-44]. Changes in serum biomarkers can reflect the onset of periodontal inflammation earlier than radiographic alterations, allowing for more timely intervention.

In summary, IL-8 and HMGB1 levels in both GCF and serum were significantly elevated in patients with chronic periodontitis compared to healthy controls, suggesting that serum IL-8 and HMGB1 levels may serve as effective biomarkers for the early detection and clinical assessment of chronic periodontitis. Furthermore, their significant reduction following basic periodontal therapy indicates a positive relationship between these inflammatory mediators and periodontal health status. However, this study has several limitations. The underlying molecular mechanisms linking IL-8 and HMGB1 to disease progression were not explored in depth, and their longitudinal behavior during different disease stages remains to be elucidated. Future studies with larger cohorts and mechanistic investigations are warranted to validate these findings and further clarify their roles in the pathogenesis of chronic periodontitis.

Table 7. Correlation analysis of serum IL-8, HMGB1 with periodontal measurements

norm	Serum IL-8		Serum HMGB1	
	r	*P-value*	*r*	*P-value*
PD (mm)	0.360	<0.0001	0.400	<0.0001
PLI	0.362	<0.0001	0.424	<0.0001
SBI	0.337	<0.0001	0.455	<0.0001
GI	0.445	<0.0001	0.530	<0.0001
CAL (mm)	0.435	<0.0001	0.532	<0.0001
Tooth mobility	0.634	<0.0001	0.698	<0.0001

Notes: GI: Gingival index, PD: periodontal probe depth, PLI: plaque index, SBI: gingival sulcus bleeding index, CAL: loss of attachment, IL-8: interleukin-8, HMGB1: high mobility group box 1.

Table 8. Correlation analysis of GCF IL-8, HMGB1 with periodontal measurements

norm	GCF IL-8		GCF HMGB1	
	r	*P-value*	*r*	*P-value*
PD (mm)	0.357	<0.0001	0.377	<0.0001
PLI	0.378	<0.0001	0.424	<0.0001
SBI	0.380	<0.0001	0.425	<0.0001
GI	0.452	<0.0001	0.497	<0.0001
CAL (mm)	0.498	<0.0001	0.527	<0.0001
Degree of looseness of teeth	0.596	<0.0001	0.643	<0.0001

Notes: GI: Gingival index, PD: periodontal probe depth, PLI: plaque index, SBI: gingival sulcus bleeding index, CAL: loss of attachment, GCF: gingival crevicular fluid, IL-8: interleukin-8, HMGB1: high mobility group box 1.

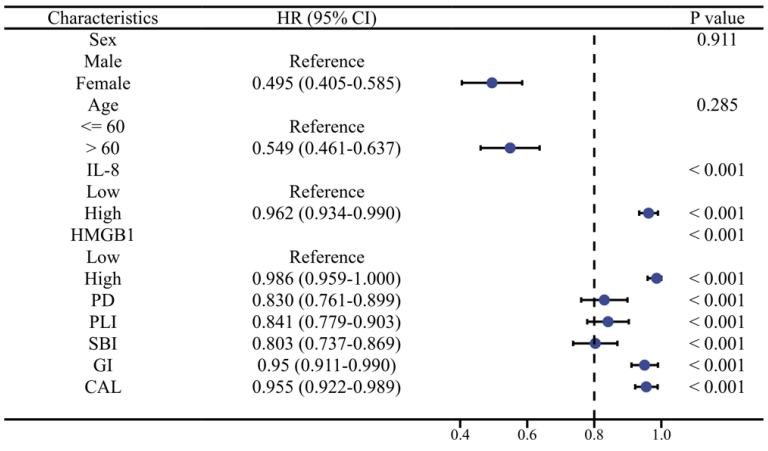

Figure 6. Multivariate Cox regression analysis of the effects of IL-8 and HGMB1 levels on chronic periodontitis severity.

Disclosure of conflict of interest

None.

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