



Interleukins 1 β and 10 Expressions in the Periimplant Crevicular Fluid From Patients With Untreated Periimplant Disease

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The long-term maintenance of osseointegration depends on the preservation of healthy marginal soft and hard periimplant tissues. Biological complications around implants were described in several studies.¹⁻⁴ In 2008, the Sixth European Workshop on Periodontology at Ittigen, Switzerland,³ discussed issues related to periimplant disease. In fact, it was observed that the most common periimplant diseases, periimplant mucositis and periimplantitis, are primarily caused by bacteria, which was confirmed in the Consensus of the Seventh European Workshop on Periodontology.⁵

Periimplant mucositis lesions are characterized as an inflammation of the mucosal cuff around the neck of a dental implant and are associated with edema,

Purpose: To analyze the interleukin (IL)-1 β and IL-10 expressions in periimplant crevicular fluid (PICF) in healthy and diseased regions to elucidate the inflammatory process around implants and its influence on clinical diagnosis.

Materials and Methods: PICF samples from 30 patients were analyzed for IL-1 β and IL-10 concentrations by enzyme-linked immunosorbent assay. Patients were divided in Groups A (health), B (mucositis), and C (periimplantitis). Plaque accumulation, periodontal phenotype (PP), depth on probing, and history of periodontitis (HP) were evaluated.

Results: IL-1 β levels were lower in healthy group compared with Groups B ($P < 0.0005$) and C ($P < 0.001$). IL-10 levels were higher in Groups A compared with

B ($P = 0.033$) and C ($P = 0.0001$). Patients with HP and thin PP had 9 and 4.5 times more chance of presenting disease, respectively.

Conclusions: Lower IL-1 β and higher IL-10 levels characterized healthy periimplant conditions, which demonstrate the anti-inflammatory predominance in sites without disease signs. IL-10 levels decrease significantly according to increase of disease status. Therefore, its levels can differentiate healthy, mucositis, and periimplantitis. Thin PP and HP are associated with periimplant disease. These findings suggest the use of ILs as a biochemical marker for early diagnosis of periimplant disease. (Implant Dent 2013;22:143-150)

Key Words: diagnosis, host mechanisms, interleukins, periimplant disease

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rubor, and bleeding on probing. Periimplantitis, a chronic progressive marginal infection, is considered to be a more advanced disease, defined as an inflammatory process affecting the tissues surrounding osseointegrated dental implants resulting in loss of supporting bone.⁶

However, because periimplantitis is caused by a bacterial challenge to the implant-bearing soft and hard tissues, the onset and the severity of the disease depend on concomitant factors specific

for the individual. Although the correlation between periodontal phenotype and periimplant disease is not well established, poor oral hygiene, tobacco abuse, and systemic medical conditions such as diabetes mellitus and history of periodontitis have been considered determinants for the increase of the incidence of the disease.³ Nevertheless, key factors for the periimplant tissue breakdown seem to be related with the local immunological reaction at the site of infection.⁷⁻⁹

Recently published research has been focused on the correlation between biochemical markers of inflammation and clinical parameters around healthy and diseased implants.¹⁰ In fact, it was shown that, in previous studies, neutrophil elastase levels have been found significantly high around failing implants when compared with healthy implants.¹¹ In addition, in mouths with failing implant sites, significantly elevated levels of interleukin (IL)-1 β have been determined as compared with healthy control implant sites.^{10,12}

The periimplant crevicular fluid (PICF) has its origin at the base of the marginal gingival sulcus, and it can be collected by different noninvasive techniques.¹³ It was shown as a promising medium for the detection of periimplant activity.¹⁴ In addition, gingival crevicular fluid has been successfully used as a biochemical marker in periodontal disease.¹⁵

Levels of biochemical mediators secreted into the PICF were considered diagnostic markers to monitor periimplant health.¹⁰ In fact, PICF seems to reflect the degree of inflammatory reaction affecting the surrounding tissues, bone and mucosae, and the presence of biomechanical stress.¹⁶

The proinflammatory cytokine IL-1 β was used as a biochemical marker of periodontal disease in clinical and *in vitro* studies,¹⁷ showing high crevicular concentrations in periodontal disease.^{18–20} In response to a periodontal or periimplant infection, IL-1 β is secreted locally to upregulate inflammatory reactions in concert with other factors of the local immune response. IL-1 β controls the extracellular matrix degradation activity of the plasminogen activator system during inflammation and wound healing.^{21,22} In addition, IL-1 β controls the production of prostaglandin E₂, which also seems to play a major role in the induction of hard tissue breakdown.^{9,23} On the other hand, IL-10 was demonstrated to be an anti-inflammatory cytokine, produced by T-helper 2 cells (T_H2), macrophages, and B cells, which inhibits synthesis of proinflammatory cytokines such as IL-1, IL2, IL6, IL8, tumor necrosis factor- α and interferon- γ . However, IL10 is a B cell stimulator, enhancing B-cell proliferation and differentiation.²⁴

Although several investigations evaluated the periimplant disease process, the relationship between inflammatory response and clinical/radiographic characteristics in healthy and diseased untreated periimplant regions seems to still be unclear. No prognostic factor for periimplant disease development has yet to be identified.²⁵

The present study aimed to analyze the expression of IL-1 β and IL-10 in the PICF in healthy and diseased periimplant regions and to correlate these levels with clinic and radiographic findings, to elucidate the inflammatory process around implants and its influence on clinical diagnosis parameters.

MATERIAL AND METHODS

Clinical study procedures were conducted according to Federal Fluminense University Research Ethical Board recommendations (Registration Number CMM/HUAP 0061.0.258.000-07). Informed consent was obtained from all the participants. Patients were told that they had the right to withdraw from the study at any time.

Patient Selection

Thirty nonsmokers partially edentulous Brazilian patients previously treated with osseointegrated endosseous implants were selected for this study from the total of patients treated in the Titanium Fix Clinical during 1 year.

They were included in this study if they were free of medical complications, were not taking medications affecting periodontal status,²⁶ were submitted to the same implant placement technique (2 stages surgery) by the same surgeon with the same implant type system (external hexagon; Titanium Fix Dental Implants; São José dos Campos, São Paulo, Brazil), had no prostheses connected and an osseointegration period between 6 and 8 months, and had immediate standard postoperative radiography showing the vertical bone level around implant to compare bone levels after osseointegration period (6–8 months after implant placement). Patients who had undergone any periodontal or periimplant therapy within the last 6 months were excluded from the study. All patients

signed a consent form after being informed of the nature of the study.

All periimplant regions were clinically and radiographically evaluated by 2 examiners, and from these, 1 periimplant region from each individual was included in this study considering the following criterions: (i) in patients presenting just 1 implant, this one was selected for clinical and laboratorial analyses and (ii) in patients presenting more than 1 implant, the periimplant tissue presenting a clinical and/or radiographic signs of disease, compatible with mucositis or periimplantitis, was selected to characterize the individual; if all periimplant regions presented healthy conditions, the implant closest to the midline was selected for analyses. Clinical examination of the periimplant sites consisted of visual inspection and palpation, analysis of mucosa color, presence of periimplant plaque accumulation, and spontaneous bleeding around implant. The periimplant sulcus was probed at 4 aspects (mesial, distal, buccal, and oral) to identify the presence of bleeding on probing, exudates, and depth on probing. Therefore, the same examiners carefully probed all regions, considering absence of pain and tactile sense based on previous report.²⁷ The probe (HuFriedy, Chicago, IL) was directed parallel to the long axis of the implant, and the presence of bleeding on probing and depth on probing were recorded. Periodontal phenotype classification according to Kao and Pasquinelli²⁸ and implant mobility were also analyzed. History of periodontitis was carefully identified in each patient by periapical radiography analysis considering aggressive or chronic periodontitis. The scores were arbitrarily chosen and ranged from 0 (no finding evident) and 1 (removable traces of adherent periimplant plaque, bleeding after pocket probing or suppuration on probing, or digital pressure to the periimplant crevice). Conventional periapical radiography, using a paralleling technique with an acrylic template, measured the presence of vertical bone loss adjacent to the implants compared with the initial radiography (just after implant placement) to standardize radiographic analysis. The height of periimplant bone was recorded according to screw exposure (range = 0–7) because all included

implants presented the same design. When more than 2 screw exposures were identified, it was considered as pathologic bone loss, and it was characterized as periimplantitis. Range 7 characterized total loss of bone/implant interface.

According to the clinical and radiographic characteristics of the periimplant sites, patients were separated into 3 groups, each containing 10 individuals. Patients in Group A (healthy sites: control group) showed no clinical signs of inflammation in the periimplant mucosa and no signs of bone loss in all regions. In Group B, periimplant sites were characterized as untreated periimplant mucositis, with the presence of bleeding on probing, red mucosa and swelling, spontaneous bleeding, but no radiographic signs of pathologic bone loss. Patients in Group C (untreated periimplantitis sites) showed clinical signs of inflammation, including implant mobility and suppuration in some cases, and radiographic signs of bone loss. All included regions were clinically and radiographically reevaluated after 1 year. Diseased regions from Groups B and C were treated as described by Jovanovic²⁹ after initial diagnosis and PICF collection.

PICF Sampling

Patients were asked to gargle with a glass of cold sterile water to cleanse the implant regions of loosely adherent debris. Subgingival samples were collected from 30 patients in duplicate at the moment of initial clinical and radiographic analysis. The area was gently air-dried and carefully isolated with cotton rolls. Samples of PICF were obtained by placing calibrated, volumetric microcapillary pipettes intracrevicularly. Pipettes in sites that did not express any volume of fluid were discarded. From each site, a standardized volume of 1 μ L was collected. The pipette was immediately rinsed in 110 μ L of phosphate-buffered saline/bovine serum albumin/1% proteases inhibitor. The solution was centrifuged for 5 min at 3000g to remove plaque and cellular elements. The samples were stored at -80° C for subsequent assays.

Enzyme-Linked Immunosorbent Assay. Levels of IL-1 β and IL-10 in all

samples were determined by using an appropriate commercial ELISA kits numbers DY201 and DY217B, respectively (kits DuoSet ELISA Development System; R&D System, Inc, Minneapolis, MN). The kits use a quantitative “sandwich” enzyme immunoassay technique. A murine antihuman monoclonal antibody specific for IL-1 β or IL-10 was precoated onto a 96-well microplate. All reagents were brought to room temperature, and assay diluent (50 μ L) was added to each well. Then, 110 μ L of the standard or the sample was added, and the plate was incubated at room temperature for 2 hours. Any IL-1 β or IL-10 present was bound by the immobilized antibody. After washing of unbound proteins, an enzyme-linked polyclonal antibody (200 μ L) specific for IL-1 β or IL-10 (goat anti-human) was added to each well. The plate was incubated at 4° C overnight, and the wells were re-washed. The 50- μ L volume of biotinylated antibody anti-IL-1 β or anti-IL-10 was added and incubated for 3 hours at room temperature. Following washing, 100 μ L of streptavidin-HRP solution was added to each well and incubated for 1 hour at room temperature. After washing, 50 μ L of a substrate solution was added to each well. The plates were incubated for 30 minutes at room temperature in the dark. The test absorbance was measured using a microplate reader at 405 nm wavelength. Concentrations in each sample were determined by generation of a standard curve and comparison with corrected PICF volume. Then, the total amount of IL-1 β or IL-10 in each sample was defined as picograms per milliliter.

Data Analyses

Individual patient data, including clinical, radiographic, and immunological characteristics, were transcribed into a statistical software program for PC (SPSS 12.0; SPSS, Inc, Chicago, IL). Clinically, the risk of developing periimplant disease was correlated to periodontal phenotype and history of periodontitis, using odds ratio (OR) with the 95% confidence interval (CI). A P value < 0.05 was considered significant. The χ^2 test was used to correlate the periimplant disease to periimplant plaque presence considering

Table 1. Baseline Characteristics of All Samples Subjects and Patients Clinical Findings

Periimplant Diagnosis	No. Individual (Male/ Female)	Patient Age (Years)	Plaque Accumulation Score*	Bleeding on Probing Score*	Pus Score*	Pocket Probing Depth (mm)†	Periodontal Phenotype		History of Chronic Periodontitis		Bone Loss‡
							Thin	Thick	Presence	Absence	
Healthy condition (Group A)	10 (3/7)	49.5	0.0	0.2	0	1.1 ± 0.5	1	9	2	8	0
Periimplant mucositis (Group B)	10 (5/5)	52.8	0.6	1.0	0.2	2.9 ± 0.5	8	2	8	2	0
Periimplantitis (Group C)	10 (4/6)	57.4	0.8	1.0	0.6	4.2 ± 1.4	10	0	10	0	5.5

Differences between diseased patients (mucositis and periimplantitis) and healthy controls as reflected by clinical and radiographic (bone loss) variables. Unit of analysis: 1 implant per patient.

*Range = 0–1.

†Mean of 4 sites measured to the nearest millimeter (mesial, distal, vestibular, and oral).

‡Range = 0–7 according to total screw exposure in radiographic analysis. More than two screw exposures = periimplantitis. Seven screw exposures = total loss of implant/bone interface.

$P < 0.05$. Differences in concentrations in IL-1 β and IL-10 levels in PICF between healthy, periimplant mucositis, and periimplantitis groups were assessed by analysis of variance. Differences in IL-1 β levels between diseased ($n = 20$) and nondiseased ($n = 10$) patients were evaluated by the Mann-Whitney test. Differences in IL-10 levels in each group was evaluated by Tukey test. The Spearman coefficient evaluated the correlation between IL-1 β and IL-10 levels in each group.

RESULTS

Thirty patients (12 women and 18 men), representing 130 osseointegrated implants (Titanium Fix Implants A.S.), with mean age 53 ± 11.8 years (range, 30–76 years), were enrolled in this study.

Clinical and Radiographic Results

Thirty implants were selected from the total of 130 implants in 30 patients (13 on mandible and 17 on maxilla). Table 1 shows the baseline clinical and radiographic aspects in each group. In Group A (healthy periimplant tissue), 2 patients (20%) presented history of chronic periodontitis, 1 patient (10%)

presented thin periodontal phenotype. No patient presented periimplant plaque accumulation, suppuration, red mucosa, or implant mobility. Bleeding on probing was observed in 2 patients, showing clinical conditions of health. Eight patients (80%) in Group B (periimplant mucositis) presented history of chronic periodontitis. Plaque accumulation around implant was present only in diseased periimplant tissues (Groups B and C). All patients in Group C presented thin periodontal phenotype around implants, history of chronic periodontitis, and bleeding on probing. The mean probing depth was 1.1 ± 0.5 mm, 2.9 ± 0.5 mm, and 4.2 ± 1.4 mm in Groups A, B, and C, respectively. Five implants with periimplantitis (Group C) presented complete bone loss around the implant and implant mobility. No patient presented history of aggressive periodontitis.

Clinical and radiographic evaluation 1 year after clinical and radiographic diagnosis, PICF sampling and treatment showed that all patients from Group A remained healthy; 2 patients from Group B showed clinical and radiographic aspects compatible with health, being transferred to group A; and 5 patients from Group C lost the implants.

Four patients from Group C had part of the bone loss recovered after regenerative treatment. However, these patients showed clinical aspects of inflammation, remaining in Group C. One patient from Group B developed aggressive bone loss, and it was transferred to Group C. All implants that were removed showed mobility at the baseline. The mean probing depth was 1.3 ± 0.5 mm, 2.3 ± 0.4 mm, and 3.6 ± 1.5 mm in Groups A, B, and C, respectively.

Correlation Between Periimplant Disease and Periodontal Phenotype. The OR analysis showed that patients with thin periodontal phenotype had 4.5 times more chance of presenting periimplant disease than patients with thick periodontal phenotype. In addition, patients characterized as thick periodontal phenotype were considered 4.5 times more resistant to periimplant disease ($P < 0.05$) (OR; 95% CI): (6.5; 1017.14).

Correlation Between Periimplant Disease and History of Periodontitis. The statistical analysis showed that patients with history of chronic periodontitis had 9 times more chance of presenting periimplant disease than patients

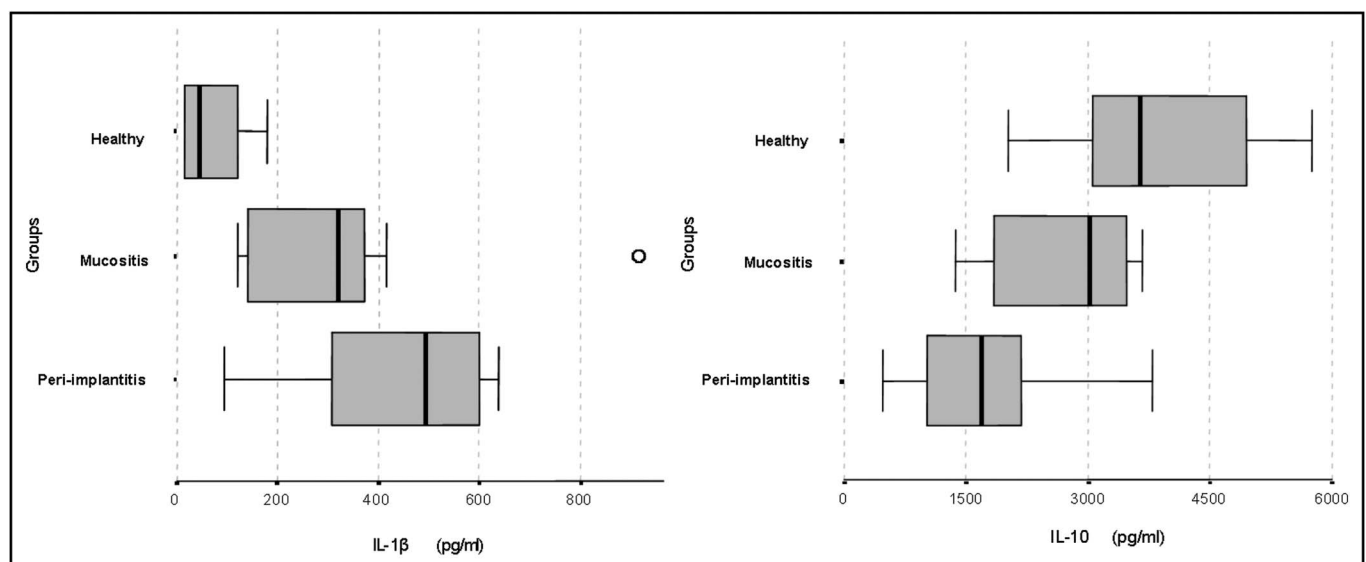


Fig. 1. Box-plot graphics showing the distribution of IL-1 β and IL-10 levels (pg/mL) in PICF from each group: healthy condition ($n = 10$), periimplant mucositis ($n = 10$), and periimplantitis ($n = 10$). Mean values (vertical black lines inside the boxes) and standard deviation are shown for each distribution. Statistical significance was calculated using ANOVA. IL-1 β levels were significantly lower in Group A (healthy) compared with Group B (mucositis) ($P < 0.0005$) and Group C (periimplantitis) ($P < 0.001$). IL-10 levels were significantly higher in healthy patients compared with Group B ($P = 0.033$) and Group C ($P = 0.0001$). Patients from Group B presented higher concentrations of IL-10 compared with Group C ($P = 0.047$).

without history of periodontitis. On the other hand, patients without history of periodontitis were 4 times more resistant to periimplant disease ($P < 0.05$) (OR; 95% CI): (4.28; 302.8).

Correlation Between Periimplant Disease and Plaque Accumulation. There was a significant association between plaque accumulation (Score 1) around implant and periimplant disease ($P < 0.001$).

Concentrations of IL-1 β and IL-10 in PICF

IL-1 β and IL-10 were detected in all samples from PICF at baseline. The mean of IL-1 β levels was significantly lower in healthy patients (67.51 ± 62.9 pg/mL) compared with Group B (mucositis, 325.89 ± 235.17 pg/mL) ($P < 0.0005$) and Group C (periimplantitis, 439.89 ± 182.67 pg/mL) ($P < 0.001$). No significant difference occurred between diseased groups ($P > 0.05$).

IL-10 levels were significantly higher in healthy patients (3720 ± 1237.97 pg/mL) compared with Group B (2711.21 ± 866.65 pg/mL; $P = 0.033$) and Group C (1707.79 ± 948.10 pg/mL; $P = 0.0001$). Patients from Group B presented higher concentration of IL-10 compared with patients from Group C ($P = 0.047$) (Fig. 1).

DISCUSSION

The present study analyzed the IL-1 β and IL-10 expressions in both healthy and untreated diseased periimplant tissues correlating these levels with clinic and radiographic findings to understand the etiopathogenesis of the periimplant disease. According to the literature, the main risk indicators described for periimplant disease development are tobacco abuse, diabetes mellitus, history of periodontitis, and poor oral hygiene.^{6,30,31} However, many cases of periimplant disease, characterized by bone loss, do not present any association with these risk indicators. Therefore, this study considered—in a clinical evaluation of the periimplant tissues—periodontal phenotype, plaque accumulation around implant, and history of periodontitis. These site specifics and individual characteristics were correlated with anti- and proinflammatory ILs (IL-10 and IL-1 β ,

respectively) in PICF as an attempt to associate these mediators to clinical features. In our study, all smoking patients were excluded to remove tobacco abuse as a risk factor or its influence on soft and hard tissue conditions.

Nevertheless, the first challenge in periimplant disease studies is the correct diagnosis of periimplantitis, which is defined as irreversible inflammatory process in the periimplant tissue with additional bone loss.³² It is important to distinguish between bone remodeling that occurs early after implant installation and the loss of supporting bone that may be detected around implants during function and can initiate just after osseointegration process or prosthesis fixation.³³ In our study, we just included patients with complete osseointegration process to identify any clinic and radiographic detectable bone alteration as loss of supporting. Then, the previous condition of osseointegration was considered for periimplant disease diagnosis. All patients were subject to the same surgery technique, using the same implant, and they were operated by the same surgeon. In addition, all patients had immediate standardized postoperative radiography documented to possibility posterior evaluation considering vertical bone loss. Other relevant aspect is the clinical diagnosis of disease. The literature discusses whether the presence of bleeding on probing is always related to periimplant collapse.^{10,33} In our study, we considered for clinical diagnosis of periimplant mucositis other aspects beyond the presence of bleeding on probing, as red mucosa color, swelling, and spontaneous bleeding. We observed that all diseased periimplant tissues show bleeding on probing but not all healthy periimplant tissues showed absence of bleeding on probing because 2 patients showed clinical and radiographic signs compatible with health bleeding on probing.

Another important question raised is if there are specific patient characteristics that may be regarded as markers for periimplantitis development. Other pertinent question is whether patients susceptible to periodontal disease have an elevated risk for developing periimplantitis and potential implant loss.³⁴ In 2008, the

relationship between history of periodontitis and periimplant disease was confirmed by Lindhe and Meyle.⁶ Our study showed that history of chronic periodontitis is a significant risk factor to periimplant disease. Patients presenting history of chronic periodontitis had 9 times more chance to develop periimplant disease than patients without history of periodontitis. In addition, plaque accumulation around implant was directly associated to the presence of periimplantitis and bone loss. We also observed that patients presenting thin periodontal phenotype had 4.5 times greater probability to present periimplant disease. On the contrary, thick periodontal phenotype worked as a protection factor against periimplant disease. However, it is important to consider that 30 patients cannot be considered to be a significant number from which to make clinical conclusions regarding risk factors such as history of periodontitis and thin periodontal phenotype. Other aspect is that thin periodontal phenotype identified in this study can be a result of bone loss and not the reason. Moreover, because of our small sample size, it is necessary for future studies to include more periimplant regions to confirm such a risk factor.

In our study, all patients from Group A maintained the periimplant tissue healthy after 1 year. These findings can corroborate with the fact that patients without history of chronic periodontitis and thick periodontal phenotype present smaller risk to develop periimplant disease. Interestingly, only 2 patients from Group B, who had no history of periodontitis and presented thick periodontal phenotype, showed clinical and radiographic aspects compatible with healthy periimplant tissue 1 year after treatment.

The fact that recent research⁶ claimed that periimplant mucositis occurs in about 80% of subjects (50% of sites) restored with implants and periimplantitis in 28% to 56% of subjects (12%–40% of sites) stimulated our research group to understand the disease process in periimplant tissues. In the present study, from a total of 130 implants, 5 implants (0.04%) were lost

in patients presenting similar clinical (thin periodontal phenotype and history of periodontitis) and laboratorial characteristics. These results can arouse the scientific community in considering the history of periodontitis and thin periodontal phenotype as important markers to periimplant disease status.

Studies showed that the presence of periodontal pathogens in periimplant sulcus will not necessarily result in periimplantitis or implant failure,^{34,35} which shows that other factors from patient (systemic and genetic factors) are involved in the survival and failure of implants. The phenomena of progressive bone loss and subsequent implant failure seem to be a result of a shift in the host-parasite equilibrium, similar to what has been observed in periodontitis.^{36,37} Increased levels of inflammatory mediators such as lactoferrin, elastase³⁷ and IL-1 β have been associated with periimplantitis.³⁸ IL-1 β production induces the release of a vast amount of inflammatory mediators, resulting in a cascade of events that lead to soft and hard tissue destruction. However, according to Hultin et al,³⁷ the correlation between IL-1 β levels and periimplantitis was not found. In our research, all samples from PICF were collected considering the real state of periimplant region, without previous treatment, to show the metabolism during disease process. We showed that healthy group was significantly different from diseased group regarding IL-1 β levels in PICF. Low levels of IL-1 β characterized, clinically and radiographically, periimplant healthy condition, whereas high levels of IL-1 β characterized clinical condition of periimplant disease. However, these high levels of IL-1 β were not able to differentiate periimplant mucositis (Group B) from periimplantitis (Group C).

Recent characterization of IL-10 as an important multifunctional cytokine has lead studies to recognize it as a key component in many aspects involving immune system.³⁹ Schierano et al,⁴⁰ in study including 11 patients, related that transforming growth factor- β 1 and IL-10 are often present in healthy mucosa around implant. These authors suggested that the induction for transforming growth factor- β 1 and IL-10 secretion

can contribute on lower inflammatory response around implant. Liskmann et al.⁴¹ evaluated IL-6 and IL-10 levels in saliva from 12 patients presenting periimplantitis and 18 healthy patients, showing that periimplantitis group presented high levels of IL-6 and IL-10. However, in their study, IL-10 was not detected in healthy group. Curiously, Duarte et al.⁴² analyzing 48 biopsies, related that IL-10 presented low expression in periimplant soft tissue biopsies from healthy implants whereas no differences were detected among the diseased groups. In contrast, our results detected IL-10 levels in PICF from healthy and diseased patients. We believe that because PICF is in close contact to bone/implant interface, it can reflect the real immunological events that occur in periimplant tissue. In addition, our results showed that IL-10 levels in PICF were important to differentiate healthy, periimplant mucositis, and periimplantitis conditions. High levels of IL-10 were compatible with healthy group, and IL-10 levels in mucositis patients were statistically higher than IL-10 levels in periimplantitis. In contrast, high levels of IL-1 β characterized disease condition but did not differentiate mucositis from periimplantitis. We observed that the clinical diagnostic of periimplantitis has correlation with low levels of IL-10. These correlations between the ILs analyzed in our study can suggest that the decrease of IL-10 can have greater influence on periimplant bone loss development than the high level of IL-1 β .

To date, no study correlated IL-1 β and IL-10 levels in PICF in patients with untreated periimplant mucositis and periimplantitis. Our findings suggest that greater the IL-10 level, lower the IL-1 β and vice versa. In healthy tissues, the high expression of IL-10 can be inhibiting the action of IL-1 β and preserving the tissue integrity. On the contrary, as observed in our study, high levels of IL-1 β were detected in disease sites together with decrease of IL-10, which mean that, in sites showing pathologic bone loss (periimplantitis sites), the disequilibrium between IL-10 and IL-1 β , with predominance of IL-1 β , triggered a destructive reaction that can be identified by clinical signs of inflammation.

The evidence that implant failures tend to increase in subsets of individuals⁴³ may indicate that specific host characteristics could disturb the osseointegration process. Increased levels of bone resorptive ILs, such as IL-1, might stimulate an excessive inflammatory response, affecting osseointegration success,²⁵ as related in our study. However, it is not clear if the regulation on anti-inflammatory cytokines, such as IL-10, can disturb the osseointegration process.^{12,39} Therefore, it seems reasonable to evaluate whether the individual's ability to produce higher or lower quantities of IL-1 β or IL-10 could influence the implant failure mechanism. This finding had a correlation with healthy mucosa, implant stability, and absence of bone loss after 1 year. We suggest that IL-1 β and IL-10 levels in PICF can be a possible diagnostic factor for periimplant disease, which needs to be confirmed with future studies having a larger number of samples.

CONCLUSIONS

Within the limits of this study, it could be concluded that a history of chronic periodontitis, plaque accumulation, and a thin periodontal phenotype are significant risk factors for periimplant disease. In contrast, a thick periodontal phenotype can act as a protection against periimplant disease. On the other hand, despite the fact that there was a limited sample, we showed that lower IL-1 β levels and higher IL-10 levels are associated, clinically and radiographically, with the health of the periimplant condition. Clinically, higher IL-1 β levels are associated with disease condition around an implant. In addition, different levels of IL-10 were able to differentiate the 3 conditions: healthy, mucositis, and periimplantitis. The expression of IL-1 β and IL-10 may play an important role in the onset and severity of periimplant disease, but further studies are necessary.

DISCLOSURE

The authors claim to have no financial interest, either directly or indirectly, in the products or information listed in the article.

ACKNOWLEDGMENTS

The first author thanks the company Titanium Fix Dental Implants (São José dos Campos, SP, Brazil) for providing clinical and laboratory components needed for this investigation.

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