LITERATURE REVIEW
INDICATORS OF BIOLOGICAL RESPONSES

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ABSTRACT

Despite the fact that dental implants have predictable outcomes and are a common technique in everyday clinical practice for oral rehabilitation, the formation and advancement of peri-implantitis has significantly harmed implant survival and success. Peri-implantitis is a well-known inflammatory condition that causes soft tissue inflammation as well as progressive bone loss that goes beyond biological osseous remodelling Importantly, earlier research has shown that the presence of periodontopathogens is necessary but not sufficient for the onset of peri-implantitis, and that osteo-immunoinflammatory mediators released by the host response have a significant impact on peri-implant tissue disintegration Given the lack of predictable and effective therapeutic interventions for the treatment of peri-implantitis scientific evidence pertaining to the host response profile around dental implants may be critical in the future for providing a wider preventive and/or therapeutic window for this peri-implant lesion, indicating biomarkers that provide quantifiable measures of response to peri-implant therapy.

KEYWORDS
Host response; Ro and anti-inflammatory mediators; Bone resorption mediators; Biomarkers;Altered response.

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Introduction

Despite the fact that dental implants have predictable outcomes and are a common technique in everyday clinical practice for oral rehabilitation, the formation and advancement of peri-implantitis has significantly harmed implant survival and success. [1][2][3] In this regard, Derks and Tomasi[4] reported in a meta-analysis study that weighted implant-based peri-implantitis prevalence was 22 percent (95 percent CI: 14–30), while another meta-analysis found that weighted implant and patient-based peri-implantitis prevalences were 9.25 percent (95 percent CI: 7.57–10.93) and 19.83 percent (95 percent CI: 15.38–24.27), respectively [5] In addition, a recent multi-level cross-sectional study found that 9.2 percent of implants (95 percent confidence interval: 4.7–13.7) and 19.1 percent of patients (95 percent confidence interval: 12.6–25.5) had peri-implantitis. Peri-implantitis is a well-known inflammatory condition that causes soft tissue inflammation as well as progressive bone loss that goes beyond biological osseous remodelling[5,6.7] Importantly, earlier research has shown that the presence of periodontopathogens is necessary but not sufficient for the onset of peri-implantitis, and that osteo-immunoinflammatory mediators released by the host response have a significant impact on peri-implant tissue disintegration [7,8] Given the lack of predictable and effective therapeutic interventions for the treatment of peri-implantitis [7–9] scientific evidence pertaining to the host response profile around dental implants may be critical in the future for providing a wider preventive and/or therapeutic window for this peri-implant lesion, indicating biomarkers that provide quantifiable measures of response to peri-implant therapy.

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Host response in patients with peri-implantitis

The importance of microorganisms in the development of peri-implant lesions is well understood, and experimental and clinical research have substantiated the cause-and-effect relationship between biofilm deposition and the development of peri-implant lesions.[10] Peri-implant tissue collapse is accompanied by a complex and well-organized microbiota that closely resembles that seen in chronic periodontitis.[11] In peri-implantitis, however, as documented by Berglundh et al.[12] based on evidence from experimental investigations[12,13] the inflammatory connective tissue penetrated surrounding implants and was connected to enhanced density of osteoclastogenic cells when compared to natural teeth.

Modulation of host osteo-immunoinflammatory mediators in peri-implantitis

Pro- and anti-inflammatory mediators

The pro-inflammatory cytokine interleukin-1 (IL-1) is mostly produced by macrophages, but it is also produced by neutrophilic granulocytes and other cells. Another pro-inflammatory signal, tumor necrosis factor (TNF), promotes the stimulation of various events, including alveolar bone loss. [12–14] The damaging impact of these mediators in periodontitis [14] is well established, and studies have also shown increased production of IL-1 and TNF- in the presentation of peri-implantitis. [15] In this regard, a meta-analysis found that TNF- and IL-1 levels in the crevicular fluid of peri-implant pockets might be used to diagnose peri-implantitis early. [16] The majority

of studies found that IL-1 was upregulated in mucositis and peri-implantitis. Additional evidence showed that IL-1 levels were linked to failing dental implants at the patient and site level, revealing a detailed profile of host response in patients with peri-implant collapse. Furthermore, IL-1 has been identified as a good option for distinguishing healthy implants from peri-implantitis. [16,17].Other cross-sectional results showed that IL-1 and IL-8 levels were significantly higher in the peri-implant crevicular fluid of peri-implantitis patients. IL-17, which is mediated by T helper 17 (Th17) cells, is another pro-inflammatory cytokine that mediates a variety of biological inflammatory effects, including neutrophil and macrophage recruitment as well as the stimulation of other pro-inflammatory pathways. [16–18] IL-23 has a critical function in enhancing Th17 responses in this situation. Treg cells, on the other hand, are characterized by increased expression of suppressive cytokines such as transforming growth factor (TGF) Interestingly, a recent study comparing the levels of IL-17, IL-23, and TGF- gene expression in healthy and diseased peri-implant tissues found a predominant Th17 response and a decrease in Treg response in the presence of peri-implantitis when compared to peri-implant healthy condition, owing to the up-regulation of IL-23 and down-regulation of TGF- in peri-implantitis tissues.[18] aimed to determine whether cytokine levels in the fluid around implants could be used to distinguish healthy implants from those with peri-implantitis, found that the majority of studies included in the review described statistically significantly higher concentrations of pro-inflammatory mediators in the peri-implant fluid of dental implants with peri-implantitis than in the peri-implant crevicular fluid of healthy implants.

Matrix metalloproteinases

The levels of matrix metalloproteinases (MMPs) like as MMP-1, MMP-7, and MMP-8 in peri-implant crevicular fluid may be affected by changes in the individual pattern of the host response. MMPs, particularly MMP-8, which is known to be the major MMP in periodontitis, play an important role in inflammatory processes by degrading extracellular matrix and basement membrane components in a variety of tissues. MMP-8, also known as collagenase-2, has been linked to the development of experimental mucositis around implants in response to plaque deposition and has been regarded as an early indicator of peri-implant breakdown [19]

Bone resorption/remodeling mediators

In the presence of lesions around dental implants, up-regulation of pro-inflammatory markers and metalloproteinases in the peri-implant tissues can also drive active osteoclast chemotaxis, altering the pattern of expression of bone resorption/remodeling mediators around the implants. In this context, previous data from a cross-sectional study showed an increased amount of C-telopeptide pyridinoline cross links of type I collagen (ICTP) in the peri-implant fluid of implants with peri-implantitis, implying increased type I collagen breakdown and bone resorption in these sites, though Tümer et al. have not confirmed significant ICTP level changes in the peri-implant sulcular fluid.

Arikan et al. found that peri-implantitis locations had considerably lower OPG and higher soluble RANKL concentrations than healthy control sites in their investigation. Furthermore, the scientists found that the RANKL/OPG ratio was higher in peri-implantitis compared to clinically healthy implants, indicating that peri-implantitis had a detrimental impact on alveolar bone resorption. Furthermore, in the peri-implantitis bone tissues, representative bone matrix biomarkers such as SPP1, BGLAP, and COL9A1 were found to be lower, whereas fibrocyte markers were found to be higher. As a result, previous research has shown that fibroblasts play a role in the etiology of peri-implantitis by upregulating vascularity and matrix breakdown. Furthermore, marginal bone loss in early experimental illnesses may create an unbalanced host response, which is thought to enhance fibroblast stimulation.

Oxidative stress biomarkers

Apart from the modulation of numerous cyto/chemokines in favor of a pro-inflammatory host response profile,peri-implant breakdown could also be linked to oxidative stress mechanisms and excessive production of reactive oxygen species, both of which have a significant impact on the host response. In this regard, Sánchez-Siles et al.evaluated the salivary concentration of oxidative stress molecules in people with peri-implantitis in a cross-sectional research. Patients with implants (four to five) diagnosed with peri-implantitis did not have high salivary malondialdehyde (MDA), a key lipid peroxidation by-product, or myeloperoxidase (MPO), the only peroxidase that catalyzes the conversion of hydrogen peroxide and chloride to hypochlorous acid concentrations.[20] It implies that peri-implantitis does not cause quantifiable oxidative stress in the saliva.However, additional prospective studies in patients with a greater number of dental implants with peri-implantitis could be important to clarify the real impact of peri-implantitis in the levels of oxidative stress molecules in saliva.

Altered peri-implant host response in patients at risk conditions

It is crucial to note that a significant number of patients undergoing dental implant therapy are those who are at risk of having an exacerbated host osteo-immunoinflammatory response to peri-implantitis-causing bacteria, such as smokers and diabetics. As a result, in certain patient profiles, a bacterial assault combined with an intensified or changed host response may contribute more easily or pronouncedly to the progression of peri-implant tissue deterioration.

Although clinical trials of dental implant success in type 2 diabetics with well-controlled glycaemia and unknown or compromised glycaemic status have shown varying failure rates with no clear relationship to glycaemic control,it has been established that poor glycaemic status is the most important factor affecting the rates of implant complications (including peri-implant bone loss) in diabetics.

Diabetic individuals have an increased risk of developing periodontitis, and poor glycaemic state may negatively modify immunological inflammatory mediators in the gingival crevicular fluid,(80) leading to periodontal attachment and tooth loss over time.[21] Furthermore, diabetes has been identified as a biological factor linked to peri-implant disorders, and results suggest that in the presence of peri-implantitis, poor glycaemic control may induce an overproduction of proinflammatory biomarkers.

According to Al-Sowygh et al.,, who studied the concentrations of advanced glycation end products (AGEs) in peri-implant crevicular fluid of type 2 diabetes mellitus patients with varying glycemic control, higher AGEs levels were also detected in patients with elevated glycemic status, implying that AGEs may be considered a probable biomarker of inflammation in diabetic subjects with peri-implantitis .Furthermore, AGE levels in peri-implant sulcular fluid were shown to be higher in patients with prediabetes, according to a recent study. When compared to individuals with normoglycemic and well-managed diabetes, Venza et al. found that type 2 diabetic patients with poorly controlled glycaemic status had overexpression of TNF- and IL-8 in peri-implantitis locations. Overall, these findings suggest

that the balance of immunoinflammatory mediators in the peri-implant fluid of diabetic patients is shifted toward hyperinflammatory characteristics, especially when glycemiccontrol is poor, potentially creating an environment conducive to peri-implant tissue breakdown over time.
TNF- and IL-1 work together to initiate critical mediators of the inflammatory cascade (Duarte et al. 2009), and these two molecules are considered the most important in osteoclast development and bone resorption.
In line, it was previously reported significantly augmented bone loss prevalence in peri-implantitis sites from poorly controlled than well-controlled diabetics or healthy patients (60.2% vs 46.3% vs 45.5%).[21,22]

-Tobacco smoking is another important factor that has been linked to an altered peri-implant host response that favours the development of peri-implantitis, increasing the prevalence of illnesses around dental implants and causing damaging peri-implant bone destruction. In this respect, multiple studies have shown that smoking affects the profile of individual host response and induces down-regulation of local osteo-immuno-inflammatory molecules around implants, even in non-manifesting inflammation locations, resulting in an increased risk of peri-implant disturbance. [21–23]

-Although there is little research on the impact of obesity on the host osteo-immunoinflammatory response, Vohra et al,[21–24] based on a cross-sectional retrospective study, found that peri-implant clinical and radiographic conditions are worse in patients with severe obesity, and suggested that this finding could be linked to an increase in the systemic low-grade inflammatory marker (C-reactive protein) in these patients.

-Impact of degradation products released from dental implants in peri-implant host immunoinflammatory response

Although their role in the etiology of peri-implantitis and the host osteo-immunoinflammatory response is still unknown, certain investigations have linked the presence of these particles to inflammatory processes [25]. Tribocorrosion product release from dental implants can be triggered by a variety of factors, including implant detachment during insertion, wear caused by micro-movements between contacting surfaces at implant/prosthetic connections, the corrosive effect of therapeutic formulations such as fluorides or bleaching agents, and peri-implantitis therapies such as implant surface polishing or implantoplasty. [26]
In an in vitro study, Irshad et al., found that peri-implant granulation tissue fibroblasts exposed to titanium dioxide (TiO2) particles in the presence of a live Porphyromonasgingivalis infection increased the pro-inflammatory response by up-regulating gene expression and TNF- production. In a similar vein, Pettersson et al. recently established in vitro that Ti ions form particles in cell culture and that IL-1 activation and secretion are linked to particles rather than soluble ions.
Other evidence suggests that soluble ions, rather than particles, are responsible for the pro-inflammatory response induced in monocytes/macrophages and the increase in the RANKL/OPG ratio, which leads to alveolar bone resorption. Taira et al. found that macrophages grown in a medium with 1 ppm titanium released 170 percent more TNF- than cells grown in a media without titanium.

Conclusion

Numerous immunoinflammatory mediators and bone-related molecules could be considered as promising biomarkers to be employed in combination with clinical evaluation for monitoring peri-implant health and disease, as shown in this study based on the available research. Monitoring host-derived biomarkers related to inflammation, such as IL-1, enzymes that degrade extracellular matrix, such as MMP-8, as well as bone loss mediators, such as RANKL, OPG, and sclerostin, whose levels are known to be altered in patients with peri-implant diseases and proposed as prognostic biomarkers in peri-implantitis, would be one possible approach. The concept of prevention, supported by early detection and rigorous maintenance therapy, could have a significant impact on peri-implant lesions.

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References

[1]. Roos-Jansåker AM, Lindahl C, Renvert H, Renvert S. Nine- to fourteen-year follow-up of implant treatment. Part I: implant loss and associations to various factors. J Clin Periodontol. 2006 Apr;33(4):283–9.
[2]. Papathanasiou E, Finkelman M, Hanley J, Parashis AO. Prevalence, Etiology and Treatment of Peri-Implant Mucositis and Peri-Implantitis: A Survey of Periodontists in the United States. J Periodontol. 2016 May;87(5):493–501.
[3]. Pimentel SP, Shiota R, Cirano FR, Casarin RCV, Pecorari VGA, Casati MZ, et al. Occurrence of peri-implant diseases and risk indicators at the patient and implant levels: A multilevel cross-sectional study. J Periodontol. 2018 Sep;89(9):1091–100.
[4]. Derks J, Tomasi C. Peri-implant health and disease. A systematic review of current epidemiology. J Clin Periodontol. 2015 Apr;42 Suppl16:S158–71.
[5]. Lee C-T, Huang Y-W, Zhu L, Weltman R. Prevalences of peri-implantitis and peri-implant mucositis: systematic review and meta-analysis. J Dent. 2017 Jul;62:1–12.
[6].Heitz-Mayfield LJA. Peri-implant diseases: diagnosis and risk indicators. J Clin Periodontol. 2008 Sep;35(8 Suppl):292–304.
[7]. Sanz M, Chapple IL, Working Group 4 of the VIII European Workshop on Periodontology. Clinical research on peri-implant diseases: consensus report of Working Group 4. J Clin Periodontol. 2012 Feb;39 Suppl 12:202–6.
[8]. Monov G, Strbac GD, Baron M, Kandler B, Watzek G, Gruber R. Soluble RANKL in crevicular fluid of dental implants: a pilot study. Clin Implant Dent Relat Res. 2006;8(3):135–41.
[9]. Jepsen S, Berglundh T, Genco R, Aass AM, Demirel K, Derks J, et al. Primary prevention of peri-implantitis: managing peri-implant mucositis. J Clin Periodontol. 2015 Apr;42 Suppl16:S152–7.
[10]. Pontoriero R, Tonelli MP, Carnevale G, Mombelli A, Nyman SR, Lang NP. Experimentally induced peri-implant mucositis. A clinical study in humans. Clin Oral Implants Res. 1994 Dec;5(4):254–9.
[11]. Rams TE, Roberts TW, Feik D, Molzan AK, Slots J. Clinical and microbiological findings on newly inserted

hydroxyapatite-coated and pure titanium human dental implants. Clin Oral Implants Res. 1991 Jul;2(3):121–7.
[12]. Berglundh T, Zitzmann NU, Donati M. Are peri-implantitis lesions different from periodontitis lesions? J Clin Periodontol. 2011 Mar;38 Suppl 11:188–202.
[13]. Lindhe J, Berglundh T, Ericsson I, Liljenberg B, Marinello C. Experimental breakdown of peri-implant and periodontal tissues. A study in the beagle dog. Clin Oral Implants Res. 1992 Mar;3(1):9–16.
[14]. Graves DT, Cochran D. The contribution of interleukin-1 and tumor necrosis factor to periodontal tissue destruction. J Periodontol. 2003 Mar;74(3):391–401.
[15]. Güncü GN, Akman AC, Günday S, Yamalık N, Berker E. Effect of inflammation on cytokine levels and bone remodeling markers in peri-implant sulcus fluid: a preliminary report. Cytokine. 2012 Aug;59(2):313–6.
[16]. Faot F, Nascimento GG, Biellmann AM, Campão TD, Leite FRM, Quirynen M. Can peri-implant crevicular fluid assist in the diagnosis of peri-implantitis? A systematic review and meta-analysis. J Periodontol. 2015 May;86(5):631–45.
[17]. Li JY, Wang H-L. Biomarkers associated with peri implant diseases. Implant Dent. 2014 Oct;23(5):607–11.
[18]. Ouyang W, Kolls JK, Zheng Y. The biological functions of T helper 17 cell effector cytokines in inflammation. Immunity. 2008 Apr;28(4):454–67.
[19]. Salvi GE, Aglietta M, Eick S, Sculean A, Lang NP, Ramseier CA. Reversibility of experimental peri-implant mucositis compared with experimental gingivitis in humans. Clin Oral Implants Res. 2012 Feb;23(2):182–90.
[20]. van der Veen BS, de Winther MPJ, Heeringa P. Myeloperoxidase: molecular mechanisms of action and their relevance to human health and disease. Antioxid Redox Signal. 2009 Nov;11(11):2899–937.
[21]. Jimenez M, Hu FB, Marino M, Li Y, Joshipura KJ. Type 2 diabetes mellitus and 20 year incidence of periodontitis and tooth loss. Diabetes Res Clin Pract. 2012 Dec;98(3):494–500.
[22]. Venza I, Visalli M, Cucinotta M, De Grazia G, Teti D, Venza M. Proinflammatory gene expression at chronic periodontitis and peri-implantitis sites in patients with or without type 2 diabetes. J Periodontol. 2010 Jan;81(1):99–108.
[23]. Ataoglu H, Alptekin NO, Haliloglu S, Gursel M, Ataoglu T, Serpek B, et al. Interleukin-1beta, tumor necrosis factor-alpha levels and neutrophil elastase activity in peri-implant crevicular fluid. Clin Oral Implants Res. 2002 Oct;13(5):470–6.
[24]. Vohra F, Al Khudhairy F, Al-Kheraif AA, Akram Z, Javed F. Peri-implant parameters and C-reactive protein levels among patients with different obesity levels. Clin Implant Dent Relat Res. 2018 Apr;20(2):130–6.
[25]. Schwarz F, Sahm N, MihatovicI, Golubovic V, Becker J. Surgical therapy of advanced ligature-induced peri-implantitis defects: cone-beam computed tomographic and histological analysis. J Clin Periodontol. 2011 Oct;38(10):939–49.
[26]. Souza JCM, Barbosa SL, Ariza EA, Henriques M, Teughels W, Ponthieux P, et al. How do titanium and Ti6Al4V corrode in fluoridated medium as found in the oral cavity? An in vitro study. Mater Sci Eng C Mater Biol Appl. 2015 Feb;47:384–93.