

## Role of interleukin-1 in peri-implantitis

Bharadwaj B<sup>1\*</sup>, Sheeja Varghese<sup>2</sup>

### ABSTRACT

**Aim:** To emphasize the etiology, microorganisms involved, pathophysiology of peri-implantitis and role of Interleukin-1 in peri-implantitis. **Background:** The survival rate of dental implants has become one of the serious issues in present day as successfully integrated implants are susceptible to disease conditions that cause loss of the implant. Although these implants are placed by periodontists, maxillofacial surgeons and prosthodontists, the maintenance of the oral cavity is completely on the patients. Poor oral hygiene subjects the surrounding tissues to inflammatory conditions similar to periodontal disease and it requires treatment. Bacterial infection causes an inflammatory response which results in bone decomposition and destruction of extracellular matrix. The above mentioned condition is peri-implantitis. **Conclusion:** Interleukin-1 $\beta$  can be used as a characteristic biomarker in peri-implantitis as it is found in gingival crevicular fluid and peri-implantitis crevicular fluid.

**KEY WORDS:** Bone suppuration, Interleukin-1, Osseointegration, Peri-implantitis

### INTRODUCTION

A dental implant is a surgical component that interfaces with the mandible and skull bones to support a dental prosthesis.<sup>[1]</sup> Dental implants fuse to bone by osseointegration.<sup>[2]</sup> Peri-implantitis is an inflammatory reaction with the loss of supporting bone in the tissues surrounding a functioning implant. Peri-implant diseases are classified according to the part of the oral tissue involved in the inflammatory process. If inflammation is located only in the gingival tissue around the implant neck, it is peri-implant mucositis. Progression of inflammation results in bone loss adjacent to the implant causing peri-implantitis.<sup>[3]</sup> Peri-implant infection results from a disturbance of the balance between the microbiological challenge and host response. If peri-implantitis is left untreated, it may ultimately lead to implant loss.<sup>[4]</sup> The American Academy of Periodontology described the presence of peri-implant mucositis as bleeding on probing (BOP) and suppuration with probing depths greater than 4 mm and no evidence of radiographic loss of bone beyond bone remodelling [5]. They described Peri-implantitis as a progressive, irreversible disease of the bone and

soft tissues around the osseointegrated dental implants under masticatory function that is accompanied by bone resorption, reduced osseointegration, deep pocket formation and suppuration.<sup>[6]</sup>

### ETIOLOGY

The various factors that cause peri-implantitis are plaque accumulation, parafunctional habits, stress, poor oral hygiene, and smoking. Two main etiological factors that significantly contribute to the onset of peri-implant mucositis and resorption of the marginal part of the bone tissue are bacterial infection and biomechanical factors, resulting from the excessive loading the implants in function. Excessive overload of implants can cause microfractures in marginal bone region and cause the loss of osseointegration around the neck of the implant, thereby leading to peri-implantitis.<sup>[7]</sup> Plaque accumulation and microbial contamination of peri-implant tissue cause inflammation of subepithelial connective tissue with massive inflammatory cell infiltrations. Epithelial seal is loosely fixed, suppuration can occur, and clinical as well radiographical signs of tissue destruction can be observed.<sup>[8]</sup>

### Microorganisms in Peri-implantitis

Dominant microorganisms isolated from the subgingival plaque in the case of peri-implantitis

#### Access this article online

Website: [jprsolutions.info](http://jprsolutions.info)

ISSN: 0975-7619

<sup>1</sup>Department of Periodontics, Saveetha Dental College, Saveetha University, Chennai, Tamil Nadu, India, <sup>2</sup>Department of Periodontics, Saveetha Dental College, Saveetha University, Chennai, Tamil Nadu, India

\*Corresponding author: Bharadwaj, Saveetha Dental College, Saveetha University, Chennai, Tamil Nadu, India. E-mail: [bharathwaj1212@gmail.com](mailto:bharathwaj1212@gmail.com)

Received on: 09-06-2018; Revised on: 14-07-2018; Accepted on: 19-08-2018

are Gram-negative bacilli and spirochetes. The number of spirochetes is directly proportional and in correlation with the quantity of plaque, pocket depth around the implants, and bone resorption. The microorganisms other than spirochetes are *Prevotella intermedia*, *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, *Actinomyces*, and *Haemophilus*.<sup>[9]</sup>

## INTERLEUKIN-1 (IL-1)

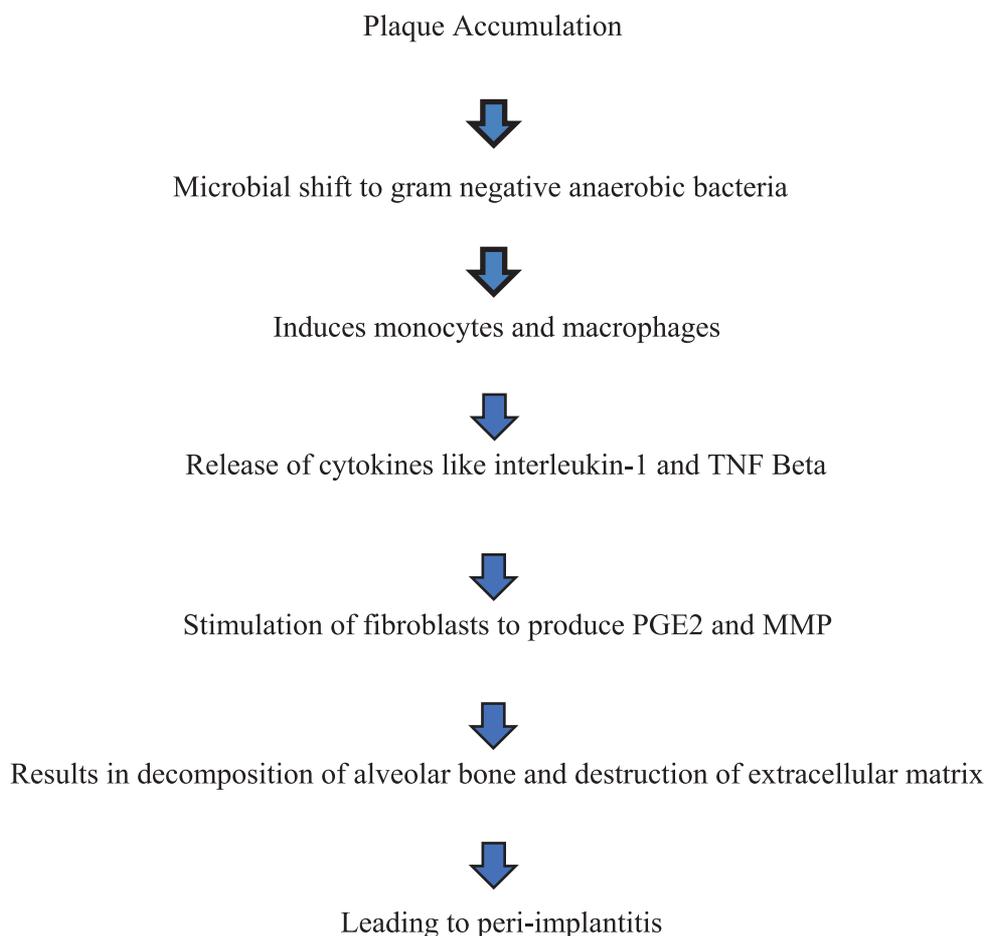
IL-1 is a group of 11 cytokines which play a key role in immune responses and inflammatory reactions to an infection. They are primarily associated with acute and chronic inflammations. The cytosolic segment of each IL-1 receptor family member contains a Toll-like receptor domain. This domain is also present in each Toll-like receptor; the receptors that respond to microbial products and viruses thereby help in providing innate immunity.<sup>[10]</sup>

### Role of IL-1 in Peri-implantitis

Peri-implantitis bacterial infection provokes immunological and biochemical response of host tissues leading to release of various cytokines.

Activation of IL-1 stimulates the connective tissue and enhances the migration of leukocytes into the tissues. This activates fibroblasts and immune nucleated cells to produce matrix metalloproteinases and prostaglandin E2.<sup>[11]</sup> Biologic effects of IL-1 depend on its tissue concentration. In periodontal tissue, IL-1 causes bone destruction and induces the production of tissue destructive proteinases.<sup>[12]</sup> Gingival crevicular fluid levels of the cytokine IL-1 were demonstrated to increase rapidly with plaque accumulation and in advance of the subsequent gingival inflammation, indicating that some cytokines may be early markers of gingival inflammatory changes.<sup>[13]</sup> In these series of events, there occurs an increase in the production of IL-1 $\beta$  by gingival macrophages, which then induces, among other things, the secretion of IL-8. These two cytokines direct selective migration of polymorphonuclear leukocytes and monocytes from the gingival blood vessels which are activated by the action of bacterial lipopolysaccharide. The progression of gingival inflammation occurs due to IL-1 $\beta$  and IL-6 activities, which cause important tissue damage by the activation of osteoclasts and induction of collagen synthesis and fibroblasts.

### Pathophysiology in peri-implantitis



<sup>[14]</sup> Pro-inflammatory cytokines such as IL-1 $\beta$  and tumor necrosis factor (TNF- $\alpha$ ) are significant in immune response to microbial antigens released by bacteria of gingival and subgingival plaque. Thus, IL-1 $\beta$  and TNF- $\alpha$  act synergistically inducing bone resorption ultimately resulting in peri-implantitis.<sup>[15]</sup>

A study done by Renvert *et al.* and Widen *et al.* revealed that there occurs a marked increase of IL-1 $\beta$  in crevicular fluid collected from patients with peri-implantitis.<sup>[16]</sup> Another study conducted by Hall *et al.* compared IL-1 $\beta$  levels in crevicular fluid of healthy individuals and peri-implantitis patients. This study showed an increase in IL-1 $\beta$  levels in peri-implantitis, whereas in healthy individuals, low level of IL-1 $\beta$  was found.<sup>[17]</sup> In few studies, peri-implant tissues were used to assess the levels of IL-1 $\beta$  are increased.<sup>[18]</sup> A study conducted by Recker *et al.* compared the level of IL-1 $\beta$  in crevicular fluid and sulcular fluid of periodontitis and peri-implantitis patients. It was found that IL-1 $\beta$  levels were in significant correlation in crevicular and sulcular fluid of a disease but varied when compared between periodontitis and peri-implantitis. This study concluded that IL-1 $\beta$  can be used as a characteristic biomarker in differentiating peri-implantitis disease from periodontitis.<sup>[19]</sup> A study conducted by Fonseca *et al.* indicated that there were no significant changes of IL-1 $\beta$  levels in saliva while it increased in crevicular fluid of peri-implantitis patients.<sup>[20]</sup> *In vitro* studies conducted by Irshad *et al.* were based on *P. gingivalis* challenge. Non-challenged fibroblasts of peri-implantitis and periodontitis showed an increased level of IL-1 $\beta$ . The *P. gingivalis* challenge induced the expression of IL-1 $\beta$  in periodontitis and peri-implantitis, whereas no significant changes were found in fibroblasts of periodontally healthy individuals. It was also found that, after removal of *P. gingivalis* challenge, fibroblasts of peri-implantitis sustained higher levels of IL-1 $\beta$  compared to fibroblasts of periodontitis.<sup>[21]</sup>

From these studies, it can be concluded that IL-1 $\beta$  gets increased in peri-implantitis. No significant changes of IL-1 $\beta$  levels in saliva of peri-implantitis were found. It can be mainly found in gingival crevicular fluid and peri-implantitis sulcular fluid. Hence, it can be used as a characteristic biomarker for peri-implantitis, and future studies are needed.

## REFERENCES

1. Perović J. Oral Implantology. Belgrade: Tekom; 2001.
2. Matic S, Stamatović N. Elements of Oral Implantology. Belgrade: Vojna štamarija; 2008.

3. Shasmitha R. Microbial profile of peri-implantitis - A review. J Pharm Sci Res 2016;8:1223.
4. Smeets R, Henningsen A, Jung O, Heiland M, Hammächer C, Stein JM, *et al.* Definition, etiology, prevention and treatment of peri-implantitis – a review. Head Face Med 2014;10:34.
5. Heitz-Mayfield LJ. Peri-implant diseases: Diagnosis and risk indicators. J Clin Periodontol 2008;35:292-304.
6. Zitzmann NU, Berglundh T. Definition and prevalence of peri-implant diseases. J Clin Periodontol 2008;35:286-91.
7. Berglundh T, Lindhe J, Lang NP. Peri-implant mucositis and peri-implantitis. In: Clinical Periodontology and Implant Dentistry. 5<sup>th</sup> ed. Oxford: Blackwell Munksgaard; 2008. p. 529-38.
8. Schou S, Holmstrup P, Worthington HV, Esposito M. Outcome of implant therapy in patients with previous tooth loss due to periodontitis. Clin Oral Implants Res 2006;17 Suppl 2:104-23.
9. Listgarten MA. Microorganisms and dental implants. J Periodontol 1999;70:220-2.
10. Weber A, Wasiliew P, Kracht M. Interleukin-1 (IL-1) pathway. Sci Signal 2010;3:cm1.
11. Andreiotelli M, Koutayas SO, Madianos PN, Strub JR. Relationship between interleukin-1 genotype and peri-implantitis: A literature review. Quintessence Int 2008;39:289-98.
12. Stashenko P, Fujiyoshi P, Obernesser MS, Probstak L, Haffajee AD, Socransky SS, *et al.* Levels of interleukin 1 beta in tissue from sites of active periodontal disease. J Clin Periodontol 1991;18:548-54.
13. Kinane DF, Winstanley FP, Adonogianaki E, Moughal NA. Bioassay of interleukin 1 (IL-1) in human gingival crevicular fluid during experimental gingivitis. Arch Oral Biol 1992;37:153-6.
14. Panagakos FS, Aboyoussef H, Dondero R, Jandinski JJ. Detection and measurement of inflammatory cytokines in implant crevicular fluid: A pilot study. Int J Oral Maxillofac Implants 1996;11:794-9.
15. Delima AJ, Oates T, Assuma R, Schwartz Z, Cochran D, Amar S, *et al.* Soluble antagonists to interleukin-1 (IL-1) and tumor necrosis factor (TNF) inhibits loss of tissue attachment in experimental periodontitis. J Clin Periodontol 2001;28:233-40.
16. Renvert S, Widén C, Persson GR. Cytokine expression in peri-implant crevicular fluid in relation to bacterial presence. J Clin Periodontol 2015;42:697-702.
17. Hall J, Pehrson NG, Ekestubbe A, Jemt T, Friberg B. A controlled, cross-sectional exploratory study on markers for the plasminogen system and inflammation in crevicular fluid samples from healthy, mucositis and peri-implantitis sites. Eur J Oral Implantol 2015;8:153-66.
18. Ata-Ali J, Flichy-Fernández AJ, Alegre-Domingo T, Ata-Ali F, Palacio J, Peñarocha-Diago M, *et al.* Clinical, microbiological, and immunological aspects of healthy versus peri-implantitis tissue in full arch reconstruction patients: A prospective cross-sectional study. BMC Oral Health 2015;15:43.
19. Recker EN, Avila-Ortiz G, Fischer CL, Pagan-Rivera K, Brogden KA, Dawson DV, *et al.* A cross-sectional assessment of biomarker levels around implants versus natural teeth in periodontal maintenance patients. J Periodontol 2015;86:264-72.
20. Fonseca FJ, Moraes Junior M, Lourenço EJ, Teles Dde M, Figueredo CM. Cytokines expression in saliva and peri-implant crevicular fluid of patients with peri-implant disease. Clin Oral Implants Res 2014;25:e68-72.
21. Irshad M, Scheres N, Moin DA, Crielaard W, Loos BG, Wismeijer D, *et al.* Cytokine and matrix metalloproteinase expression in fibroblasts from peri-implantitis lesions in response to viable porphyromonas gingivalis. J Periodontol Res 2013;48:647-56.

Source of support: Nil; Conflict of interest: None Declared