ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)

IJDSIR : Dental Publication Service

Available Online at: www.ijdsir.com

Volume – 2, Issue – 4, July – August - 2019, Page No. : 117 - 125

Expression of Bio Markers Sclerostin and IL-6 in Crevicular Fluid around Implants and Natural Teeth

Dr. Pragya, Post Graduate Student, Department of Periodontics, Faculty of Dental Science, M. S. Ramaiah University of Applied Sciences, Bengaluru-560054

Dr.Kranti Konuganti, Professor, Department of Periodontics, Faculty of Dental Science, M. S. Ramaiah University of Applied Sciences, Bengaluru-560054

Dr.Ashwini, Professor & HoD, Department of Periodontics, Faculty Of Dental Science, M. S. Ramaiah University of Applied Sciences, Bengaluru-560054

Corresponding Author: Dr.Kranti Konuganti, Professor, Department of Periodontics, Faculty of Dental Science, M. S. Ramaiah University of Applied Sciences, Bengaluru-560054

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Introduction: Dental Implants are imperative therapeutic modality for replacement of missing teeth. Peri-implant pathologies are also highly prevalent these days and effect peri-implant hard and soft tissues. So the aim of the study was to estimate the level of bone biomarker Sclerostin and IL-6 in Peri-Implant Sulcular Fluid (PISF) and find its association with peri implants status

Material and methods: In this study, 20 patients who were due for prosthetic phase of implant procedure were selected according to inclusion and exclusion criterias. After 15-20 days of loading of implant and after 3 months of implant loading, PISF and Gingival Crevicular fluid (GCF) were collected and stored at - 80^0 C. Similarly, Clinical parameters were also recorded at baseline and 3 months. Immuno- histochemical analysis of the stored PISF and GCF samples was performed and individual values were recorded for every patient.

Results: Statistically significant increase in level of Sclerostin was noted at 3 months which correlated with values of clinical parameter.

Conclusion: The results of the study revealed increased Sclerostin level in PISF when compared to its level in GCF. Thus biochemical analysis of PICF was identified as a potential diagnostic aid for Peri-Implantitis.

Keywords: Sclerostin, Peri-Implant Sulcular Fluid, Dental Implants.

Introduction

Contemporary dentistry counts oral implant as an imperative therapeutic modality for replacement of missing teeth. It has been used for replacement of lost natural teeth in periodontally sound as well as the compromised patients. Peri-implant pathologies are also highly prevalent these days. They may effect either the peri-implant mucosa alone (Peri-implant mucositis) or both peri-implant soft and hard tissues (Peri Implantitis).1There are variety of tools to evaluate peri-implant health, like radiographs, bleeding on probing, probing pocket depth around implant and quantitative and qualitative assessment of Peri implant sulcular fluid. Current studies have pointed out the utility of Peri-implant sulcular fluid (PISF) as a valuable diagnostic aid for detecting early stages of peri-implant pathologies.2

A biomarker is defined as a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic process, or pharmacologic responses to a therapeutic intervention. Biomarkers present an attractive and promising diagnostic tool in oral implantology because they have the ability to provide real-time information about ongoing processes affecting bone metabolism, and, as such, they are able to compensate for some of the shortcomings of other diagnostic aids.3,4 Therefore, biomarkers may be considered as a potential diagnostic solution with the ability to compensate for limitations of routine clinical tools and thus Peri implant sulcular fluid can be the most important diagnostic marker for the health of a dental implant.5,6,7

IL-6 is one of the most common biomarker located at the site of peri-implant inflammation. IL-6 has been identified in PISF/GCF collected from diseased periodontal/peri-implant sites and a correlation between IL-6 concentration and clinical parameter of disease has also been established.8,9 Hence, IL-6 can be used as a standard biomarker while establishing correlation between level of a relatively new biomarker and clinical level of disease progression.10,11

Sclerostin is a marker of mature osteocytes and affects bone metabolism by inhibiting osteoblast differentiation. It is believed to act by promoting osteoclast formation via a RANKL-dependent pathway and by interacting with osteoblasts.12 Its expression, which suppresses osteoblastogenesis and reduces the viability of osteoblasts and osteocytes, leads to unbalanced bone turnover in favor of bone resorption.13,14

Thus, level of such inflammatory cytokines, Bone biomarkers, Enzymes, Proteins and other constituents of PISF can be assessed to diagnose peri-implant disease conditions.

Material and Methods

Twenty Patients were recruited from the outpatient Department of Periodontology. The ethical clearance for the present study was obtained from the ethical committee of the institution. This was an interventional, follow up study. Patients aged 20-50 years healthy patients with no allergies or metabolic bone disease, no history of antibiotic use in the prior 3 months , patients who underwent surgical phase of implant placement 3 months before and are due for implant loading , healthy implant site before loading and at least one healthy tooth present adjacent to the implant were included .Patients with Chronic Periodontitis , Peri implantitis or bone loss after implant placement with systemic diseases and mobile implant presenting with incomplete osseointegration were excluded from the study .

Sample size was estimated by using Mean Sclerostin levels as 146.16 ± 95.83 from the study by Rakic, Struillou, Petkovic-Curcin, et al. At 5% alpha error and 95% power a sample size of 20 was obtained considering 249.7 as the null hypothesis value. 20 patients who were due for prosthetic phase of implant procedure were selected according to inclusion and exclusion criterias. Informed consent was obtained from all the selected patients. After 15-20 days of loading of implant, Peri-Implant Sulcular Fluid (PISF) from the implant sulcus and Gingival Crevicular fluid (GCF) from the tooth sulcus were collected and stored at - 80^0 C. At the same time Clinical Parameters such as Probing pocket depth, Clinical attachment level, Plaque Index, Papillary bleeding index were also recorded. The same was repeated again after 3 months. Level of IL-6 and Sclerostin was assessed in the stored PISF and GCF samples at the end of the study using ELISA and the individual values (tooth and implant) were recorded for every patient. Collection and analysis of GCF and PISF samples: GCF was collected from the

sulcus around the tooth adjacent to implant by placing a capillary tube parallel to the tooth surface for 30 seconds inside the sulcus after proper isolation using cotton rolls. The Samples were then transferred to the vials and mixed with Phosphate buffer saline to attain a neutral pH. The same was then stored at -78 ^{0}C until all the samples were collected after 3 months follow up. PISF was collected from the sulcus around implant by placing a capillary tube parallel to the implant surface for 30 seconds inside the sulcus after proper isolation using cotton rolls. The Samples were then transferred to the vials and mixed with Phosphate buffer saline to attain a neutral pH. The same was then stored at -78 ^{0}C until all the samples were collected after 3 months follow up.ELISA kits of Sclerostin and IL-6 were used to analyse the concentration in GCF and PISF. The kits used a double-antibody sandwich enzyme-linked immunosorbent one-step process assay (ELISA) to assay the level of Sclerostin and IL-6 in samples.

Results

The study population consisted of twenty patients, ten (50%) of them were males and ten (50%) were females. 35 % of the study population was within the age range of 31-40 years, another 35% within 51-60 years, 15% each in the age range of 41-50 years and ≤30 years .The mean Plaque index was 1.03 mm at baseline and 1.19 mm at 3 months with mean difference of -0.16 mm between the two time intervals and this difference was not found to be statistically significant as the p value was found to be 0.07. Papillary bleeding index was 1.39 at baseline and 1.50 at 3 months with a mean difference of -0.11 mm between the two time intervals and this difference was also not found to be statistically significant as the p value was found to be 0.09.Highly statistically significant difference with a p-value of <0.001 was noted in Probing pocket depth between baseline and 3 months (Mean of 2 mm at baseline and 3.25 mm at 3 months with a mean difference of -1.25). Similarly, highly statistically significant difference with a p-value of <0.001 was noted in Clinical attachment level also between baseline and 3 months (mean of 2.65 mm at baseline and 3.70 mm at 3 months)The change in level of IL-6 from baseline to 3 months around tooth was found to be statistically significant (P value <0.001) , with a mean of 5.67 pg/ml at baseline and 7.78 pg/ml at 3 months and mean difference of -2.11 pg/ml between the 2 time periods.At implant site also, this difference was found to be statistically significant (P-value <0.001) , the mean value at baseline being 9.26 pg/ml and 11.75 pg/ml at 3 months with a mean difference of -2.50 pg/ml.(Table 1, Graph 1). At baseline there was statistically significant difference P-value <0.001 noted between the levels of IL-6 at tooth (5.67 pg/ml) and implant site (9.26 pg/ml) with a mean difference of -3.59 pg/ml. At 3 months there was statistically significant difference P-value <0.001 noted between the levels of IL-6 at tooth (7.78 pg/ml) and implant site (11.75 pg/ml) with a mean difference of -3.98 pg/ml (Table 2, Graph 2) Statistically significant increase in the level of sclerostin was noticed from baseline to 3 months around tooth (mean sclerostin level of 126.63 pg/ml at baseline around tooth, 172.88 pg/ml at 3 months around tooth) with a mean difference of -46.25 and p-value P value <0.001.Statistically significant increase in the level of sclerostin was noticed from baseline to 3 months at implant site (mean sclerostin level of 178.61 pg/ml at baseline around implant, 229.13 pg/ml at 3 months around implant) with a mean difference of -50.52 and p-value P value <0.001.At baseline there was statistically significant difference P-value <0.001 noted between the levels of Sclerostin at tooth (29.60 pg/ml) and implant site (31.48 pg/ml) with a mean difference of -51.98 pg/ml. At 3 months there was statistically

significant difference P-value <0.001 noted between the levels of Sclerostin at tooth (172.88 pg/ml) and implant site (229.13 pg/ml) with a mean difference of -56.25 pg/ml.

Correlation between clinical and biochemical parameter: Very weak correlation was seen between level of IL-6 at tooth and implant site at baseline and 3 months and clinical parameters (PI, PBI, PPD ,CAL) (r value=0.01-0.20).

Very weak correlation was seen between level of Sclerostin at tooth and implant site at baseline and clinical parameters (PI,PBI,PPD,CAL) and level of sclerostin at 3 months around tooth and Papillary bleeding index (r value=0.01- 0.20).Weak correlation was found between level of Sclerostin at 3 months around tooth and implant site and plaque index (r value=0.20 - 0.40)Moderately Strong correlation was noted between level of Sclerostin at 3 months around tooth site and PPD, CAL. A similar moderately Strong correlation was noted between level of Sclerostin at 3 months around implant site and PPD, CAL and Papillary Bleeding Index (Graph 3, Graph 4).

Discussion

Peri-Implantitis is a multifactorial disease with the presence of pathogenic bacteria being necessary for the initiation of inflammation, but the progression of peri-Implant disease depends equally on the host response to various pathogenic bacterial products and components.

15,16The complex cytokine network that mediates the immune response includes pro-inflammatory cytokines, anti-inflammatory cytokines, specific cytokine receptors and bone biomarkers.

Bone biomarkers are considered more promising in cases of Peri-imaplantitis because of numerous evidences which suggest higher manifestation of bone biomarkers in PISF compared to GCF. Also, literature suggests that most of the studies conducted on assessment of level of bone biomarkers in PISF are either cross sectional in nature or they have been conducted on group of patients already diagnosed with peri-implantitis.17, 18, 19 This is one of the first studies where patients were followed up from the prosthetic phase of their implant treatment and clinical and biochemical status of their Periodontal and Peri-implant area was evaluated and correlated over 3 months.20,21

The present study was conducted with an aim to evaluate level of biomarkers Sclerostin and IL-6 around implant and tooth at baseline and 3 months and correlate the same with clinical status of tooth and implant area.

The results of this study revealed no statistically significant change in values of plaque index and papillary bleeding index from baseline to 3 months. This was in aggrement with a study by *Mauro Dunatti et al, 2008* which found no significant difference in amount of plaque after 3 and 12 months of implant loading. [22] Another study by *Ingvaar Ericsson, 2000* reported decreased mean bleeding index from baseline to 6 months of implant loading.23 In this study, Mean Probing pocket depth and Clinical attachment level was found to be significantly increased at 3 months from prosthetic phase of implant therapy. This was in accordance with a study by *U.Bragger et al, 1996* where clinical parameters of Probing attachment level was assessed along with other biochemical and radiographic parameters at 1,3,6,12 and 24 months of loading and a definite increase in clinical values correlating with biochemical and radiographic parameter was noted at 3,6 and 12 months.24,25,26

Another study by *Mauro Dunatti et al, 2008* reported a mean marginal bone loss of 0.31 mm, 0.25 mm and 0.38 mm in three treatment groups within 12 months of implant loading and also reported that the overall marginal bone loss over the entire 12-month period were almost similar to those reported for the first 3 months.27,28 This is supposed to be the reason behind increase In Probing

Pocket Depth and Clinical attachment level at the end of 3 months in the present study.The reason for this early bone loss after implant loading has been assessed by *Tae-Ju Oh et al, 2002*. It was stated that early crestal bone loss is often observed after the first year of function, followed by minimal bone loss (≤ 0.2 mm) annually thereafter. Six plausible etiologic factors were hypothesized, including surgical trauma, occlusal overload, peri-implantitis, microgap, biologic width, and implant crest module.29

Like GCF, PISF is known to contain host-derived enzymes and their inhibitors, inflammatory mediators, and tissue breakdown products.These fluids are considered particularly attractive in the diagnostic realm because of the non-invasive collection methods and the fact that they contain molecules whose levels may reflect both local and systemic inflammation. A study by *D. Dolanmaz et al, 2014* reinforced the diagnostic value of PISF but stating that considering the correlations between clinical and biochemical parameters, the levels of cytokines in PICF during early healing of implants reflects the degree of peri-implant inflammation.30 A constant higher value of both the biomarkers were noted at Implant site when compared to tooth site in this study. Also stronger positive correlation was seen between the level of one of the two biomarkers (Sclerosdtin) in PISF and clinical parameters (PPD, CAL, PBI) when compared to level of GCF and clinical parameters in this study. Thus biochemical analysis of PICF was identified as a potential diagnostic aid for Peri-Implantitis. This finding was supported by a study conducted by Erica et al, 2014 in which significant positive correlations were noted between the concentrations of cytokines in PISF versus their levels in GCF and it was concluded that PISF is a more precise diagnostic marker when compared to GCF.31

Similarly in a study by Fernanda Faot et al, 2015 it was deduced that PICF containing inflammatory mediators, can be used as additional criteria for a more robust diagnosis of peri-implant infection. It was also braced by Farhan Durrani et al, 2015 that PISF have a considerable diagnostic potential as it exhibits the biologic changes around load bearing endosseous dental implants.32

Interlekin-6 (IL-6) is an inflammatory mediator involved in bone resorption. A recent review by Javed F et al, 2011 nicely summarized human clinical trials showing that sites affected with peri-implantitis exhibited higher levels of IL-1b, TNF-a, IL-6, and IL-8 compared with healthy controls.

Apart from peri-implantitis, PISF samples taken from implant sites with peri-implant mucositis also exhibited significantly higher IL-6 levels compared with healthy sites according to a study by *Ata-Ali J, 2013.* Considering the above mentioned evidences, IL-6 can be considered an established standard biomarker of peri-implantitis and thus it was included in the study for standardisation in assessing the correlation of level a relatively new biomarker sclerostin with change in clinical parameters.

In the present study it was found that the level of IL-6 was constantly higher at Implant site when compared to the tooth site. This was in accordance with a study by Hessam Nowzari et al, 2008 where it was concluded that the concentration of IL-6 was more prominent around implants than teeth, reaching nearly two fold difference in some instances.

Sclerostin is a marker of mature osteocytes and affects bone metabolism by inhibiting osteoblast differentiation. It is believed to act by promoting osteoclast formation via a RANKL-dependent pathway and by interacting with osteoblasts. Although there are many bone biomarkers, Umut Balli, 2015 concluded in his study that GCF sclerostin level may be more reliable than the RANKL/OPG ratio as a diagnostic and prognostic marker of periodontal disease and treatment outcome.33

Regulation of sclerostin levels may aid the development of new therapeutic strategies for the treatment of periodontal disease better than OPG or RANKL and thus it was the chosen as biomarker of interest in this study.

This study reports Moderately Strong correlation between level of Sclerostin at 3 months around tooth site and PPD, CAL. A similar moderately Strong correlation was noted between level of Sclerostin at 3 months around implant site and PPD, CAL and Papillary Bleeding Index.This finding of the present study is supported by the establishment that SOST/sclerostin has been identified in cementocytes and is known to have a role in mineralizing periodontal ligament cells in a histological study by A. Jger et al, 2009

Conclusions

Within the limitations of this study it is plausible to suggest that Sclerostin can be a potential biomarker for identification of Periodontal and Peri-implant disease status. Similar multinodal studies on larger sample size with Longer follow up period is recommended for assessing the peri-implant condition and disease progression.

References

1. Rakic M., Struillou X , Petkovic-Curcin, A, Matic S, Canullo L, Sanz M, et al. Estimation of bone loss biomarkers as a diagnostic tool for peri-implantitis. J Periodontol 2014; 85(11): 1566-1574.
2. Wohlfahrt J.C, Aass A.M., Granfeldt F, Lyngstadaas, S.P, Reseland, J.E. Sulcus fluid bone marker levels and the outcome of surgical treatment of peri-implantitis. J Clin Periodontol 2014; 41(4):424-431.
3. Onuma T, Aquiar K, Duarte P.M, Feres M,Giro G, Coelho P et al Levels of Osteodastogenesis-Related Factors in the Peri-Implant Crevicular Fluid and Clinical Parameters of Immediately Loaded Implants in Patients with Osteopenia: A Short-Term Report. Int J Oral Max Imp 2015, 30(6),214-219
4. Recker, E.N., Avila-Ortiz, G., Fischer, C.L., Pagan-Rivera, K., Brogden, K.A., Dawson, D.V.et al , A cross-sectional assessment of biomarker levels around implants versus natural teeth in periodontal maintenance patients. J Periodontol 2015, 86(2), 264-272.
5. Alan R., Marakoğlu İ, Haliloğlu S. Peri-implant crevicular fluid levels of cathepsin-K, RANKL, and OPG around standard, short, and mini dental implants after prosthodontic loading. J Periodontal Implant Sci, 2015; 45(5):169-177.
6. Canullo L, Orlato Rossetti P.H, Penarrocha D. Identification of Enterococcus Faecalis and Pseudomonas Aeruginosa on and in Implants in Individuals with Peri-implant Disease: A Cross-Sectional Study. Int J Oral Max Imp 2015; 30(3):919-28
7. Paolantonio M, Di Placido G, Tumini V, Stilio M.D, Contento A, Spoto G. A spartate Aminotransferase Activity in Crevicular Fluid from Dental Impiants. J Periodontol 2000; 71(7):1151-57.
8. Thierbach R, Maier K, Sorsa T, Mäntylä P. Peri-Implant Sulcus Fluid (PISF) Matrix Metalloproteinase (MMP)-8 Levels in Peri-Implantitis. J Periodontol 2016;25:943-6
9. Faot F, Nascimento G.G, Bielemann A.M, Campão T.D, Leite F.R , Quirynen, M, Can peri-implant crevicular fluid assist in the diagnosis of peri-implantitis? A systematic review and meta-analysis. J Periodontol 2015; 86(5):631-45
10. Ertugrul A.S, Tekin Y, Alpaslan N.Z, Bozoglan A, Sahin, H, Dikilitas A Comparison of peri-implant crevicular fluid levels of adrenomedullin and human beta defensins 1 and 2 from mandibular implants with

different implant stability quotient levels in nonsmoker patients. J Periodontol Res 2014; 49(4):480-88.

11. Vieira A , Moura C.C.G, De Souza M.A, Zanetta-Barbosa D, Dechichi P. Would nitric oxide be an effective marker for earlier stages of peri-implant disease? An analysis in human peri-implant sulcular fluid. J Oral Implantol 2013; 39(1):37-43.
12. Ramseier C.A, Eick S, Brönnimann C, Buser D, Brägger U, Salvi, G.E Host-derived biomarkers at teeth and implants in partially edentulous patients. A 10-year retrospective study. Clin Oral Implants Res 2016;65:155-68
13. Dolanmaz D, Saglam M., Inan, O, Dundar N, Alniacık G, Gursoy Trak Bet al Monitoring bone morphogenetic protein-2 and-7, soluble receptor activator of nuclear factor-κB ligand and osteoprotegerin levels in the peri-implant sulcular fluid during the osseointegration of hydrophilic-modified sandblasted acid-etched and sandblasted acid-etched surface dental implants. J Periodontal Res 2015;50(1):62-73
14. Janska E., Mohr B, Wahl G. Correlation between peri-implant sulcular fluid rate and expression of collagenase2 (MMP8). Clin Oral Inv 2015:1-6.
15. Durrani F, Singh R. Myeloperoxidase level around dental implants as an indicator of an inflammatory process. Indian J Dent 2015;6(1):2-6
16. Wohlfahrt J.C, Aass A.M., Granfeldt F, Lyngstadaas, S.P, Reseland J.E. Sulcus fluid bone marker levels and the outcome of surgical treatment of peri-implantitis. J Clin periodontol 2014; 41(4):424-431.
17. Jäger A, Götz, W, Lossdörfer S, Rath-Deschner B. Localization of SOST/sclerostin in cementocytes in vivo and in mineralizing periodontal ligament cells in vitro. J Periodontol Res 2010; 45(2):246-254.
18. Ren, Y, Han, X, Ho, S.P, Harris S.E, Cao Z, Economides A.N, Qin, C. Removal of SOST or blocking its product sclerostin rescues defects in the periodontitis mouse model. FASEB J, 2015; 29(7):2702-711.
19. Babel N, Cherepnev G, Babel D, Tropmann, A, Hammer M, Volk H.D. Analysis of tumor necrosis factor-α, transforming growth factor-β, interleukin-10, IL-6, and interferon-γ gene polymorphisms in patients with chronic periodontitis. J Periodontol 2006; 77(12):1978-1983.
20. Severino V.O, Napimoga M.H, Lima Pereira S.A. Expression of IL-6, IL-10, IL-17 and IL-8 in the peri-implant crevicular fluid of patients with peri-implantitis. Arch Oral bio 2011; 56(8): 823-28.
21. Balli U, Aydogdu A, Dede F.O, Turer C.C, Guven, B. Gingival crevicular fluid levels of sclerostin, osteoprotegerin, and receptor activator of nuclear factor-κB ligand in periodontitis. J Periodontol 2015; 86(12):1396-1404.
22. Nicoli L.G, Oliveira G.J.P.L.D, Lopes B.M.V, Marcantonio C, Zandim-Barcelos D.L. Survival/Success of Dental Implants with Acid-Etched Surfaces: A Retrospective Evaluation After 8 to 10 Years. Braz Dent J 2017; 28(3):330-336.
23. Xu L, Yu Z Lee H.M, Wolff M.S, Golub L.M., Sorsa T, Kuula H. Characteristics of collagenase-2 from gingival crevicular fluid and peri-implant sulcular fluid in periodontitis and peri-implantitis patients: pilot study. Acta Odontol Sca 2008; 66(4):219-24
24. Trevilatto P.C, Scarel-Caminaga R.M, De Brito R.B, De Souza A.P, Line, S.R.P. Polymorphism at position− 174 of IL-6 gene is associated with susceptibility to chronic periodontitis in a Caucasian Brazilian population. J Clin Periodontol; 2003 30(5):438-42.

25. Reis C, Da Costa A.V, Guimarães J.T, Tuna D, Braga A.C, Pacheco J.J et al Clinical improvement following therapy for periodontitis: Association with a decrease in IL-1 and IL-6. Ex Ther Med 2014; 8(1):323-27.
26. Nowzari H., Botero J.E, DeGiacomo M., Villacres M.C,Rich S.K. Microbiology and cytokine levels around healthy dental implants and teeth. Clin Implant Dent Relat Res 2008; 10(3):166-173.
27. Geivelis, M., Turner, D.W., Pederson, E.D. and Lamberts, B.L.,. Measurements of interleukin-6 in gingival crevicular fluid from adults with destructive periodontal disease. J Periodontol 1993; 64(10):980-83.
28. Lamster I.B, Ahlo J.K... Analysis of gingival crevicular fluid as applied to the diagnosis of oral and systemic diseases. Ann NY Aca Sci, 2007; 1098(1):216-229.
29. Oh T.J, Yoon J, Misch, C.E, Wang H.L. The causes of early implant bone loss: myth or science? J Periodontol 2002; 73(3):322-333.
30. Donati M., La Scala, V, Billi, M, Di Dino B, Torrisi, P, Berglundh T. Immediate functional loading of implants in single tooth replacement: a prospective clinical multicenter study. Clin Oral Implants Res 2008; 19(8): 740-48.
31. Renouard F, Nisand, D. Short Implants in the Severely Resorbed Maxilla: A 2-Year Retrospective Clinical Study. Clin Implant Dent Relat Res 2005;7:353-8
32. Ericsson I, Nilson H, Lindh T, Nilner K, Randow, K. Immediate functional loading of Brånemark single tooth implants. Clin Oral Implants Res 2006; 11(1):26-33.
33. Laney W.R., Jemt T, Harris D, Henry P.J, Krogh P.H, Polizzi G et al Osseointegrated implants for single-tooth replacement: progress report from a multicenter prospective study after 3 years. Int J Oral Maxillofac Implants 1994; 9(1):116-119

Legends Tables and Figure

Comparison of mean values of Bio-markers IL-6 & Sclerostin levels between baseline and 3 month time interval using Student Paired t test

Parameters	Time	N	Mean	SD	Mean Diff	t	P-Value
IL6_Tooth	Baseline	20	5.67	2.57	-2.11	-4.247	<0.001*
	3 Months	20	7.78	2.26			
IL6_Implant	Baseline	20	9.26	2.77	-2.50	-3.814	0.001*
	3 Months	20	11.75	2.85			
SCL_Tooth	Baseline	20	126.63	29.60	-46.25	-9.066	<0.001*
	3 Months	20	172.88	28.41			
SCL_Implant	Baseline	20	178.61	31.48	-50.52	-6.294	<0.001*
	3 Months	20	229.13	33.46			

*P<0.05 is Statistically Significant. SCL-Sclerostin

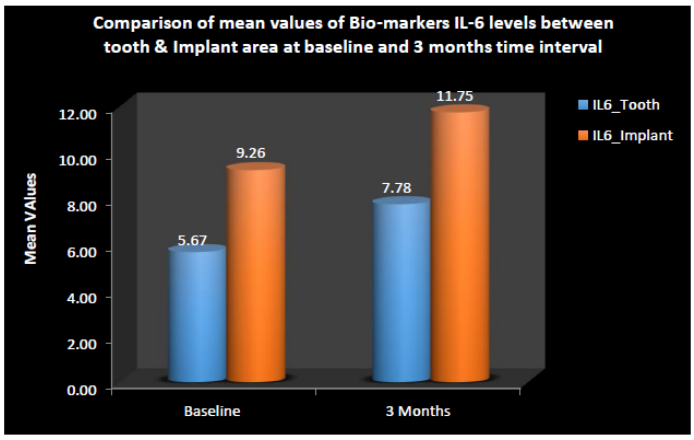
Table 1: Comparison of mean values of Bio-markers IL-6 and Sclerostin levels between baseline and 3 months' time interval

Comparison of mean values of Bio-markers IL-6 & Sclerostin levels between tooth & Implant area at baseline and 3 months time interval using Student Paired t test

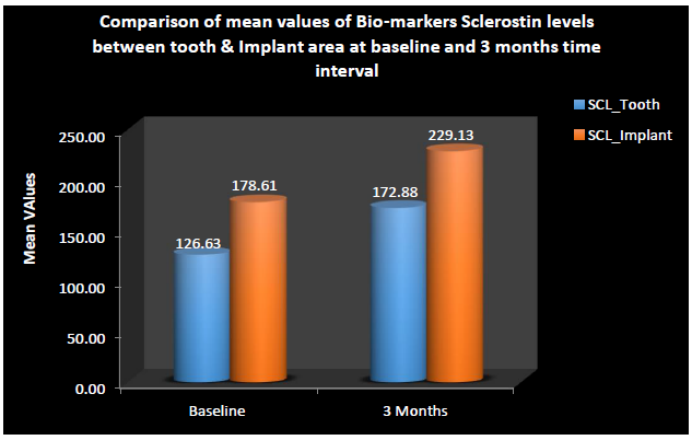
Parameters	Time	N	Mean	SD	Mean Diff	t	P-Value
Baseline	IL6_Tooth	20	5.67	2.57	-3.59	-7.244	<0.001*
	IL6_Implant	20	9.26	2.77			
3 Months	IL6_Tooth	20	7.78	2.26	-3.98	-8.293	<0.001*
	IL6_Implant	20	11.75	2.85			
Baseline	SCL_Tooth	20	126.63	29.60	-51.98	-8.807	<0.001*
	SCL_Implant	20	178.61	31.48			
3 Months	SCL_Tooth	20	172.88	28.41	-56.25	-11.686	<0.001*
	SCL_Implant	20	229.13	33.46			

*P<0.05 is Statistically Significant. SCL-Sclerostin

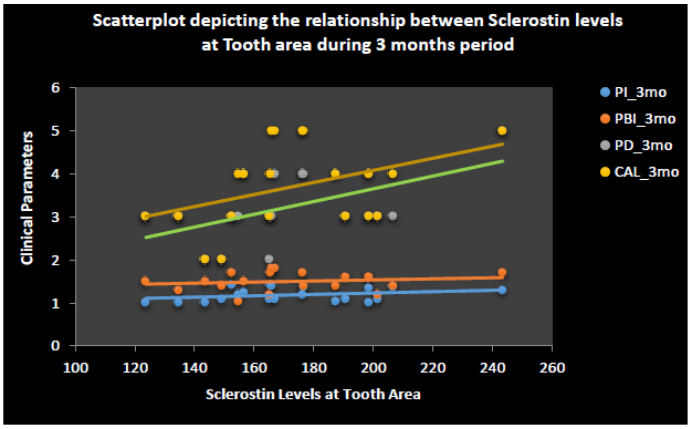
Table 2: Comparison of mean values of Bio-markers IL-6 and Sclerostin levels between tooth and implant area at baseline and 3 months' time interval



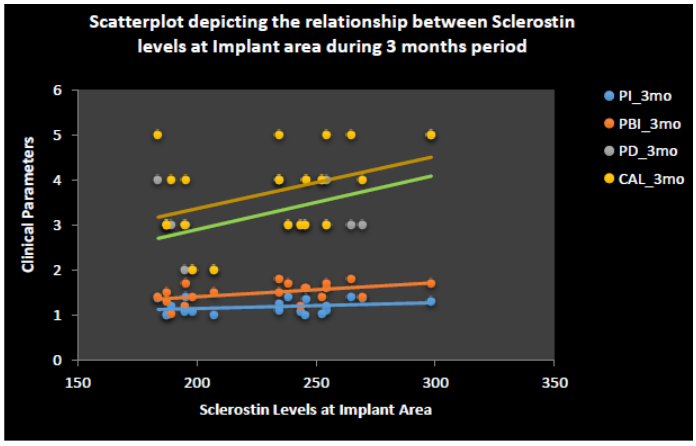
Graph 1 : Comparison of mean values of bio-markers IL-6 levels between tooth and implant area at baseline and 3 months time interval



Graph 2: Comparison of mean values of bio-markers Sclerostin levels between tooth and implant area at baseline and 3 months time interval



Graph 3: Scatterplot depicting relationship between Sclerostin at tooth area during 3 months period



Graph 4: Scatterplot depicting relationship between Sclerostin at implant area during 3 months period

Legends

Table 1: Comparison of mean values of Bio-markers IL-6 and Sclerostin levels between baseline and 3 months time interval

Table 2: Comparison of mean values of Bio-markers IL-6 and Sclerostin levels between tooth and implant area at baseline and 3 months time interval

Graph 1 : Comparison of mean values of bio-markers IL-6 levels between tooth and implant area at baseline and 3 months time interval

Graph 2: Comparison of mean values of bio-markers Sclerostin levels between tooth and implant area at baseline and 3 months time interval

Graph 3: Scatterplot depicting relationship between Sclerostin at tooth area during 3 months period

Graph 4: Scatterplot depicting relationship between Sclerostin at implant area during 3 months period