Original Article

EFFECT OF MECHANICAL DEBRIDEMENT ON CLINICAL PARAMETERS AND PICF TWEAK LEVELS AMONG PERI-IMPLANTITIS DISEASE PATIENTS: A 1-YEAR STUDY

*Rupak Mario[1], Arvina Rajasekar[2]**

[1]*Department of Implantology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India.*
[2]*Department of Periodontology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India.*
arvinar.sdc@saveetha.com

Received: 17 July 2026; **Revised:** 30 September 2026; **Accepted:** 07 October 2026 https://doi.org/10.51847/GrZTeviBrP

ABSTRACT

Peri-implantitis is an inflammatory disease that compromises peri-implant tissue health and human wellbeing. Host-mediated cytokines such as tumor necrosis factor-like weak inducer of apoptosis (TWEAK) play a role in tissue destruction, highlighting their relevance in oral medicine and public health. To evaluate the effect of mechanical debridement on clinical parameters and peri-implant crevicular fluid (PICF) TWEAK levels in peri-implantitis patients. In this prospective interventional study, 54 systemically healthy patients with peri-implantitis underwent mechanical debridement. Peri-implant probing depth (PPD), clinical attachment loss (CAL), and PICF TWEAK levels were assessed at baseline, 6 months, and 1 year. Repeated measures ANOVA with Bonferroni correction was used for analysis. Significant reductions in PPD, CAL, and PICF TWEAK levels were observed at 6 months, and 1 year compared to baseline ($p < 0.001$), indicating progressive clinical and biochemical improvement. Mechanical debridement improved peri-implant health and significantly reduced PICF TWEAK levels. TWEAK may serve as a potential biomarker for monitoring inflammatory disease activity and therapeutic response, supporting strategies aimed at promoting oral health and overall wellbeing.

Key words: Biomarker, Cytokine, Disease, Peri-implant disease, Wellbeing.

Introduction

Dental implants have gained widespread acceptance as a predictable and long-term therapeutic modality for the rehabilitation of partially and completely edentulous patients, with continuous advancements in biomaterial science and surface engineering enhancing clinical outcomes [1-4]. Furthermore, emerging computational and bioinformatic approaches have identified key genetic regulators and molecular pathways involved in peri-implant bone formation and remodeling, reflecting the growing integration of precision medicine concepts into implant dentistry [5, 6].

Despite these technological advancements, peri-implantitis remains a significant biological complication affecting implant longevity. The pathogenesis of peri-implantitis is initiated by biofilm accumulation but is primarily driven by a dysregulated host immune-inflammatory response [7]. A complex network of cytokines, chemokines, and osteoclastogenic mediators orchestrates connective tissue breakdown and alveolar bone resorption around dental implants [8-10]. Therefore, identification of molecular biomarkers reflecting disease activity and therapeutic response has become an area of growing interest in peri-implant research.

Tumor necrosis factor-like weak inducer of apoptosis (TWEAK), a member of the tumor necrosis factor superfamily, is a multifunctional cytokine involved in inflammation, angiogenesis, cell proliferation, and apoptosis [11]. Through binding to its receptor fibroblast growth factor-inducible 14 (Fn14), TWEAK activates intracellular signaling pathways such as NF-κB and MAPK, leading to upregulation of proinflammatory mediators and adhesion molecules [12]. Experimental and clinical evidence suggests that TWEAK contributes to periodontal tissue inflammation and may participate in bone remodeling processes by influencing osteoclast activity [13]. Elevated levels of TWEAK have been reported in inflammatory conditions affecting both oral and systemic tissues, indicating its potential relevance as a biomarker.

Peri-implant crevicular fluid (PICF), analogous to gingival crevicular fluid around natural teeth, represents a valuable diagnostic medium as it reflects the local inflammatory status of peri-implant tissues. Cytokine quantification within PICF provides a less invasive way to track the course of the disease and the effectiveness of treatment [14]. However, longitudinal data evaluating changes in PICF TWEAK levels following non-surgical peri-implant therapy remain limited.

Mechanical debridement remains the cornerstone of non-surgical peri-implantitis management, aiming to disrupt biofilm and reduce inflammatory burden [15]. While clinical parameters are routinely used to assess treatment success, incorporation of biochemical markers may provide

© 2026 Annals of Dental Specialty. **Open Access** – This Article is licensed under CC BY NC SA 4.0. To view a copy of this license, visit https://creativecommons.org/licenses/by-nc-sa/4.0/

deeper insight into the underlying host response. Therefore, the present prospective interventional study was designed to evaluate the effect of mechanical debridement on clinical parameters and PICF TWEAK levels over a one year period in patients with peri-implantitis, and to explore the potential role of TWEAK as a biomarker of disease activity and therapeutic response.

Materials and Methods

Study design

The Department of Periodontology at Saveetha Dental College and Hospitals in Chennai, India, was the site of this prospective interventional trial. 54 individuals with peri-implantitis who were systemically healthy and between the ages of 30 and 60 were included. Only mechanical debridement was administered to each individual. The Saveetha University Institutional Ethics Committee granted ethical approval, and prior to enrollment, each subject provided written informed consent. G*Power software (Version 3.1.9.4) was used to calculate the sample size (n = 54) based on previously published data [16].

At least one functional dental implant with radiographic and clinical indications of peri-implantitis was necessary for inclusion. Exclusion criteria included tobacco use (current or former), pregnancy or lactation, systemic conditions, intake of antibiotics or other medications within the last six months, and a history of periodontitis or prior peri-implant therapy.

Intervention protocol

All participants underwent full-mouth ultrasonic scaling. Implant surface debridement was performed using titanium curettes (Hu-Friedy®, Chicago, USA) by a single operator (RM) to ensure consistency.

Clinical assessment

Clinical parameters, including peri-implant probing depth (PPD) and clinical attachment loss (CAL), were measured at six sites per implant: mesio-buccal, mid-buccal, disto-buccal, mesio-lingual/palatal, mid-lingual/palatal, and disto-lingual/palatal. Clinical assessment was performed by a single calibrated examiner (AR) at baseline, 6 months, and 1 year. Mean values for each parameter were calculated for analysis.

Sample collection

Prior to PICF collection, supragingival plaque was removed using a sterile curette, and the implant site was isolated with sterile cotton rolls. PICF samples were gathered using calibrated microcapillary pipettes under standardized protocols and promptly stored at −20°C prior to biochemical evaluation. To maintain consistency, all collections across the baseline, 6-month, and 1-year intervals were performed by a single examiner (AR).

Quantification of PICF TWEAK

TWEAK concentrations were measured using a commercially available Human TWEAK ELISA kit (Elabscience®, Houston, TX, USA) following a sandwich ELISA protocol. Microplate wells pre-coated with a monoclonal antibody specific to human TWEAK were incubated with standards and samples to allow binding. A biotin-conjugated detection antibody and avidin-horseradish peroxidase were sequentially added, followed by washing. A chromogenic substrate was introduced, producing a blue color in wells containing the antigen-antibody complex, which turned yellow upon stopping the reaction. Absorbance readings were taken at 450 ± 2 nm via a microplate reader. TWEAK levels, quantified in pg/mL using a standard reference curve, spanned a detection range of 7.81–500 pg/mL. Data collection occurred at baseline, 6 months, and 1 year.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS), Version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables, including PPD, CAL, and PICF TWEAK concentrations, were expressed as mean ± standard deviation (SD). To evaluate temporal shifts in these variables, a repeated measures ANOVA was utilized, subsequently paired with Bonferroni-corrected post hoc comparisons to pinpoint significant variations across distinct time intervals. Statistical significance was established at a threshold of $p < 0.05$.

Results and Discussion

A total of 54 participants were included in the study, with a mean age of 45.3 ± 8.2 years. The gender distribution was 28 males (51.9%) and 26 females (48.1%). All participants completed the 1-year follow-up.

The longitudinal evaluation of peri-implant parameters is presented in **Table 1**. PPD decreased significantly from 5.85 ± 0.12 mm at baseline to 4.01 ± 0.05 mm at 6 months, and further to 3.57±0.03 mm at 1 year ($p < 0.001$, repeated measures ANOVA). Similarly, CAL showed a significant reduction from 5.97 ± 0.10 mm at baseline to 4.15 ± 0.04 mm at 6 months and 3.68±0.02 mm at 1 year ($p < 0.001$). PICF TWEAK concentrations demonstrated a significant and progressive reduction from 212.39 ± 35.02 pg/mL at baseline to 53.78 ± 10.01 pg/mL at 6 months, reaching 48.14±9.13 pg/mL at 1 year ($p < 0.001$).

Table 1. Clinical, and biochemical outcomes over time in peri-implantitis patients post-mechanical debridement

Parameter	Baseline (Mean ± SD)	6 Months (Mean ± SD)	1 year (Mean ± SD)	p-value (Repeated Measures ANOVA)	Post hoc Pairwise Comparison (Bonferroni)
PPD (mm)	5.85±0.12	4.01±0.05	3.57±0.03	<0.001*	Baseline vs 6 months: <0.001*;

					Baseline vs 1 year: <0.001*; 6 months vs 1 year: 0.002*
CAL (mm)	5.97±0.10	4.15±0.04	3.68±0.02	<0.001*	Baseline vs 6 months: <0.001*; Baseline vs 1 year: <0.001*; 6 months vs 1 year: 0.001*
TWEAK (pg/mL)	212.39±35.02	53.78±10.01	48.14±9.13	<0.001*	Baseline vs 6 months: <0.001*; Baseline vs 1 year: <0.001*; 6 months vs 1 year: 0.04*

*Statistically Significant

Post hoc pairwise comparisons indicated that for all parameters, there were significant differences between baseline and 6 months, baseline and 1 year, and between 6 months and 1 year, demonstrating a consistent and progressive improvement in clinical, and biochemical outcomes following mechanical debridement **(Table 1)**.

Peri-implantitis remains a significant biological complication affecting implant longevity. While inflammatory mediators are known to contribute to peri-implant tissue breakdown, longitudinal evidence evaluating specific cytokine modulation following non-surgical therapy is limited. In particular, data on peri-implant crevicular fluid TWEAK dynamics after mechanical debridement are scarce. Therefore, this prospective interventional study assessed changes in clinical parameters and PICF TWEAK levels over a one-year period in patients with peri-implantitis.

The findings of this study demonstrated a statistically significant and progressive reduction in PPD, and CAL from baseline to six months, with further improvement at 1 year. Parallel to these clinical improvements, PICF TWEAK concentrations showed a marked decline over time. Post hoc comparisons confirmed significant differences between all evaluated time points, indicating that mechanical debridement resulted not only in clinical resolution of inflammation but also in measurable modulation of the local cytokine milieu.

The biological plausibility of these findings is supported by earlier investigations exploring TWEAK in periodontal tissues. Kataria *et al*. [17] reported increased expression of TWEAK and its receptor Fn14 in periodontitis-affected gingival tissues compared to healthy controls, highlighting its contribution to periodontal inflammation and bone loss. Similarly, Hosokawa *et al*. [18] demonstrated that TWEAK stimulates gingival fibroblasts to produce proinflammatory mediators and enhances adhesion molecule expression, thereby facilitating leukocyte recruitment and sustaining inflammatory cascades. These mechanistic insights corroborate the observed reduction in PICF TWEAK levels following disruption of the microbial biofilm in the present study.

More directly related to peri-implant disease, Yakar *et al*. [19] reported elevated levels of TWEAK, RANKL, and sclerostin in peri-implantitis compared to peri-implant health, suggesting their potential as biomarkers of peri-implant tissue breakdown. This aligns closely with the elevated baseline TWEAK levels observed in our peri-implantitis cohort and their subsequent decline following therapy.

Therapeutic biomarker studies in periodontal settings further reinforce these observations. Yilmaz *et al*. [20] demonstrated dynamic changes in salivary TWEAK and macrophage-associated proteins following non-surgical periodontal treatment, indicating responsiveness of this pathway to mechanical therapy. Similarly, Gur *et al*. [21] and Erduran *et al*. [22] reported significant reductions in TWEAK levels after scaling and root planing, with or without adjunctive laser application. These findings collectively support the role of TWEAK as a treatment-responsive inflammatory mediator.

Systemic investigations add broader context to the inflammatory relevance of TWEAK. Leira *et al*. [23] identified associations between periodontitis and elevated circulating soluble TWEAK levels in patients with vascular inflammatory conditions. Likewise, Pradeep *et al*. [24] demonstrated increased TWEAK concentrations in both crevicular fluid and serum in advanced periodontitis and diabetes mellitus, underscoring its involvement in both local and systemic inflammatory networks. Although the present study focused exclusively on local PICF levels, these systemic associations further substantiate the biological significance of TWEAK in chronic inflammatory diseases.

Collectively, mechanical debridement resulted in significant clinical improvement along with a sustained reduction in PICF TWEAK levels, supporting its role in the inflammatory pathway of peri-implantitis and its responsiveness to therapy. The study's novelty lies in its prospective longitudinal design assessing PICF TWEAK exclusively in peri-implantitis patients over six months, providing temporal evidence of biomarker modulation following standardized treatment. Methodological strengths include strict inclusion criteria, a single calibrated examiner, standardized intervention, and repeated measures analysis, enabling reliable evaluation of both clinical and biochemical outcomes.

Limitations

Limitations include the absence of a parallel control group, modest sample size, evaluation of a single cytokine, and lack of longitudinal radiographic assessment. Future randomized controlled trials with larger cohorts, broader biomarker

panels, and correlation with radiographic bone changes are warranted to further validate these findings.

Conclusion

Mechanical debridement produced significant clinical improvement in peri-implantitis patients, accompanied by a marked reduction in PICF TWEAK levels over 1 year. The parallel decline in clinical parameters and TWEAK concentrations suggests that TWEAK may serve as a potential local biomarker for monitoring inflammatory status and therapeutic response in peri-implant disease. Further controlled studies are needed to confirm its clinical applicability.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: The study protocol was approved by Institutional Ethical Board of Saveetha Dental College and Hospitals, Chennai, India.

References

1. Maiti S, Dhakshinya M, Nallaswamy D, Jessy P. Comparative analysis of surface characteristics and hardness of three-dimensional printed PEEK vs PEKK as implant biomaterial. J Osseointegr. 2024;16(1):16-22.
2. Nahata B, Maiti S, Ganesh MK, Heboyan A, Sai L, Paulraj J. Sulfonated polyether ketone ketone (SPEKK) implant as an alternative to titanium implant—in vivo study on Wistar Albino rat mandible. BMC Oral Health. 2025;25(1):557.
3. Royapuram Parthasarathy P, Anaiambalam Tharmar MA, Thangavelu L. Ceramic biomaterials in dental implantology—time for change of status quo: an updated review. World J Dent. 2024;15(8):733-42.
4. Devarakonda S, Subramanian AK, Sivashanmugam P. Surface characterization of strontium phosphate coating on magnesium for bioimplant applications: a preliminary in vitro study. World J Dent. 2024;15(3):208-13.
5. Yadalam PK, Sharma S, Natarajan PM, Ardila CM. Gradient boosting-based classification of interactome hub genes in periimplantitis with periodontitis—an integrated bioinformatic approach. Front Oral Health. 2024;5:1462845.
6. Yadalam PK, Ardila CM. Deep neural networks based on Sp7 protein sequence prediction in peri-implant bone formation. Int J Dent. 2025;2025:7583275.
7. Alves CH, Russi KL, Rocha NC, Bastos F, Darrieux M, Parisotto TM, et al. Host-microbiome interactions regarding peri-implantitis and dental implant loss. J Transl Med. 2022;20(1):425.
8. Chakraborty P, Rajasekar A. Inflammatory and antioxidant status in peri-implant health and diseases: a biochemical analysis. J Long Term Eff Med Implants. 2025;35(2):77-81.
9. Cinderella R, Rajasekar A. Unveiling alpha amylase dynamics in peri-implant crevicular fluid: a comparative analysis across peri-implant health and disease spectrums. J Long Term Eff Med Implants. 2025;35(3):91-6.
10. Oliveira JA, de Oliveira Alves R, Nascimento IM, Hidalgo MA, Scarel-Caminaga RM, Cristina Pigossi S. Pro- and anti-inflammatory cytokines and osteoclastogenesis-related factors in peri-implant diseases: systematic review and meta-analysis. BMC Oral Health. 2023;23(1):420.
11. Potrovita I, Zhang W, Burkly L, Hahm K, Lincecum J, Wang MZ, et al. Tumor necrosis factor-like weak inducer of apoptosis-induced neurodegeneration. J Neurosci. 2004;24(38):8237-44.
12. Burkly LC, Michaelson JS, Hahm K, Jakubowski A, Zheng TS. TWEAKing tissue remodeling by a multifunctional cytokine: role of TWEAK/Fn14 pathway in health and disease. Cytokine. 2007;40(1):1-6.
13. Vincent C, Findlay DM, Welldon KJ, Wijenayaka AR, Zheng TS, Haynes DR, et al. Pro-inflammatory cytokines TNF-related weak inducer of apoptosis (TWEAK) and TNFα induce the mitogen-activated protein kinase (MAPK)-dependent expression of sclerostin in human osteoblasts. J Bone Miner Res. 2009;24(8):1434-49.
14. Alassy H, Parachuru P, Wolff L. Peri-implantitis diagnosis and prognosis using biomarkers in peri-implant crevicular fluid: a narrative review. Diagnostics (Basel). 2019;9(4):214.
15. Muthukuru M, Zainvi A, Esplugues EO, Flemmig TF. Non-surgical therapy for the management of peri-implantitis: a systematic review. Clin Oral Implants Res. 2012;23:77-83.
16. de Mendonça AC, Santos VR, César-Neto JB, Duarte PM. Tumor necrosis factor-alpha levels after surgical anti-infective mechanical therapy for peri-implantitis: a 12-month follow-up. J Periodontol. 2009;80(4):693-9.
17. Kataria NG, Bartold PM, Dharmapatni AASK, Atkins GJ, Holding CA, Haynes DR. Expression of tumor necrosis factor-like weak inducer of apoptosis (TWEAK) and its receptor, fibroblast growth factor-inducible 14 protein (Fn14), in healthy tissues and in tissues affected by periodontitis. J Periodontal Res. 2010;45:564-73.
18. Hosokawa Y, Hosokawa I, Ozaki K, Nakae H, Matsuo T. Proinflammatory effects of tumour necrosis factor-like weak inducer of apoptosis (TWEAK) on human gingival fibroblasts. Clin Exp Immunol. 2006;146(3):540-9.
19. Yakar N, Guncu GN, Akman AC, Pınar A, Karabulut E, Nohutcu RM. Evaluation of gingival crevicular fluid and peri-implant crevicular fluid levels of sclerostin,

TWEAK, RANKL and OPG. Cytokine. 2019;113:433-9.
20. Yilmaz M, Demir E, Gürsoy M, Firatli E, Loimaranta V, Gürsoy UK. Salivary levels of BAFF, TWEAK, and soluble CD163 and salivary arginase activity before and after periodontal treatment. J Periodontal Res. 2023;58(3):646-54.
21. Gur AT, Guncu GN, Akman AC, Pinar A, Karabulut E, Nohutcu RM. Evaluation of GCF IL-17, IL-10, TWEAK, and sclerostin levels after scaling and root planing and adjunctive use of diode laser application in patients with periodontitis. J Periodontol. 2022;93(8):1161-72.
22. Erduran NE, Guncu GN, Akman AC, Acar B, Pinar A, Karabulut E, et al. Evaluation of the effect of adjunctive diode laser application on peri-implant crevicular fluid biomarker levels: a randomized controlled trial. Clin Oral Investig. 2024;28(8):459.
23. Leira Y, Ameijeira P, Domínguez C, López-Arias E, Ávila-Gómez P, Pérez-Mato M, et al. Severe periodontitis is linked with increased peripheral levels of sTWEAK and PTX3 in chronic migraineurs. Clin Oral Investig. 2020;24(2):597-606.
24. Pradeep AR, Jayan A, Debnath K. TWEAK, IL-6 and MMP-9: novel biomarkers linking stage III Grade B periodontitis and type 2 diabetes mellitus. Asian Pac Soc Periodontol. 2023;6(1):30.