Original Article

ANALYSIS OF CLINICAL PARAMETER AND TUMOR NECROSIS FACTOR-ALPHA LEVELS ON KERATINIZED TISSUE AROUND IMPLANT AND TOOTH

Sofia Meier[1], *Leon Baumann*[1]*

[1]*Department of Periodontology and Fixed Prosthodontics, University of Berne, School of Dental Medicine, Berne, Switzerland. leon_baumann@gmail.com*

Received: 10 November 2024; **Revised:** 27 February 2025; **Accepted:** 27 February 2025 https://doi.org/10.51847/wFJob9BRVY

ABSTRACT

Studies have shown the importance of keratinized tissue around implants to prevent peri-implant diseases. This study aims to analyze the correlation of keratinized tissue around implants and teeth with clinical parameter scores and tumor necrosis factor-alpha (TNF-α) levels. A cross-sectional study of 20 adults with 20 dental implants and 20 contralateral teeth that have functioned suprastructurally for more than 3 months without any systemic diseases. Keratinized tissue around implant and tooth was measured. The clinical examinations included the plaque index (PI), papilla bleeding index (PBI), and pocket depth (PD). Peri-implant sulcus fluid (PISF) and gingival crevicular fluid were collected to measure TNF-α levels. Spearman's test was used to analyze the correlation. Significant differences were found between keratinized tissue around the implant in PI, PBI, and PD ($P < 0.05$). Differences were found between wide and narrow keratinized tissue around contralateral teeth in PI and PBI ($P < 0.05$) but not in PD. TNF-α levels were not correlate to keratinized tissue width around implant and contralateral tooth ($P > 0.05$). Strong correlations were found between each clinical parameter score and the keratinized tissue width of peri-implant tissue in PI, PBI, and PD. The clinical parameter score between wide and narrow keratinized tissue around implant showed strong correlation, particularly in PBI. This shows the importance of adequate keratinized tissue around implant to maintain implant stability.

Key words: Clinical parameter, Keratinized tissue, Peri-implant, Tumor necrosis factor-alpha

Introduction

The increase in dental implant treatments today as a treatment of choice for replacing missing teeth has led to increased patient expectancy regarding the treatment results. However, failure and complications in dental implant treatments have also increased [1–14]. Papaspyridakos *et al*. classified the criteria for implant treatment success based on the implant level, peri-implant soft tissue level, prosthetic level, and patient satisfaction level [4, 15-17]. Studies have shown the importance of keratinized tissue around an implant to prevent peri-implant diseases [3, 5, 18–28]. Implant success can be assessed using clinical and immunological examinations [6, 8, 19, 29, 30]. Peri-implant sulcular fluid (PISF) may contain biomarkers to diagnose and predict future diseases. Studies show that the highest level of biomarkers found in peri-implant diseases was tumor necrosis factor-alpha (TNF-α) [1, 31–34]. This study aims to analyze the correlation of keratinized tissue around an implant and tooth with clinical parameter scores and TNF-α levels.

Materials and Methods

This work is a cross-sectional study of dental implants and their contralateral teeth. The subjects were patients who underwent dental implant placement at the dental hospital during the recall program. The participants were 20 adults aged 17–60-year-old with at least one loaded dental implant that functioned suprastructurally for more than 3 months and its contralateral tooth. The sample size was calculated using the formula for estimating the sample size in the analytic-bivariate-comparative test. All participants gave their informed consent to participate in this study and were seen by two examiners. Subjects with systemic diseases were excluded.

The keratinized tissue width around the implant–tooth was measured from the free gingival margin to the mucogingival junction on the mid-buccal using a UNC-15 probe [35]. The measurement of the width of the keratinized tissue was classified into two groups according to Lang and Löe: Group I, which has a keratinized width of <2 mm (narrow), and Group II, which has a keratinized width of ≥2 mm (wide) [36].

The keratinized tissue phenotype was examined using transparencies when the probe was inserted into the sulcus and subsequently divided into two groups: thick and thin phenotypes [37]. The clinical parameter score was evaluated using the plaque index (PI), papilla bleeding index (PBI), and pocket depth (PD) [23, 35]. The peri-implant status was measured using a titanium or plastic implant probe to avoid damaging the peri-implant tissue. The immunological condition was evaluated by collecting peri-implant sulcus fluid (PISF) and gingival crevicular fluid (GCF) from the

sulcus using sterile paper points number 40 and then inserting them into a tube containing a physiological solution of phosphate-buffered saline. The TNF-α level was determined using the enzyme-linked immunosorbent assay test. For proper isolation, cotton rolls were used in the buccal and lingual areas of the study site before sample collection [19, 20, 38, 39].

IBM SPSS Statistics v22, New York, USA was used for the statistical analysis to calculate all the parameter outcomes. The groups were compared for the two-site within-participant design. The measurements at the implant site–contralateral tooth site were calculated, and independent *t*-tests were performed to determine the difference between the groups. Spearman's correlation analysis was performed to evaluate the strength and direction of the correlation. **Figure 1** shows the mechanism of the research from sample collection to data analysis.

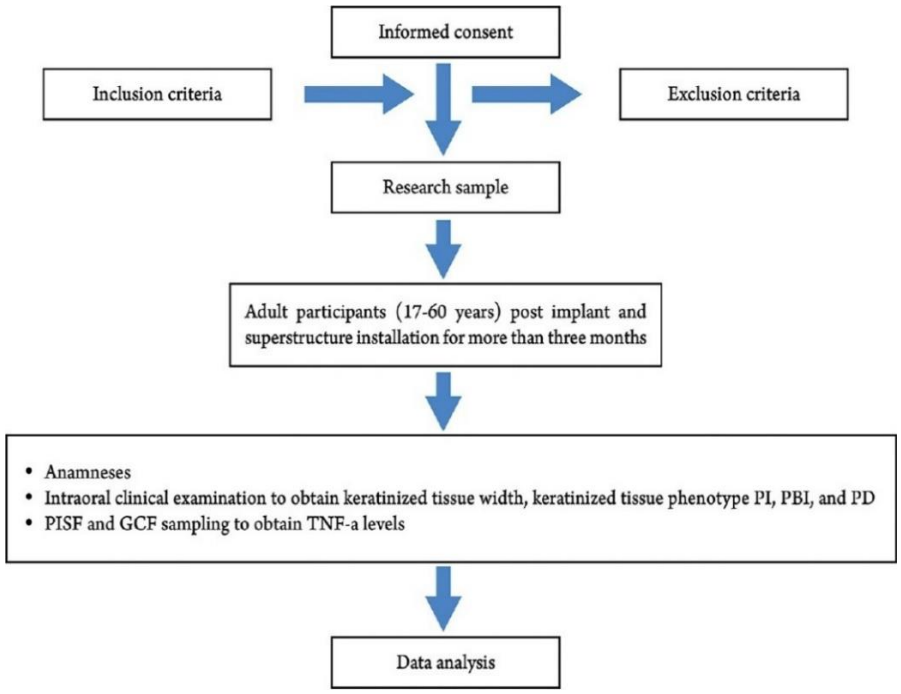


Figure 1. Diagram showing the mechanism of sample collection. TNF-α – Tumor necrosis factor alpha, PI – Plaque index, PBI – Papilla bleeding index, PD – Pocket depth, PISF – Peri implant sulcular fluid, GCF – Gingival crevicular fluid

Results and Discussion

The proportion of wide and narrow keratinized tissue was relatively equal on both the implant and the contralateral tooth. All the samples collected had a thick phenotype in the posterior region. All implant designs found in the study were at the bone level. Most of the implant samples had an adjacent tooth (75%), a medium implant diameter (65%), a medium-length (60%), and cement-retained prosthesis (75%) **(Tables 1 and 2)**.

Table 1. Proportion of subjects based on peri-implant keratinized tissue characteristics

Keratinized tissue characteristics	*n*	Proportion (%)
Keratinized tissue width (mm)		
Narrow (<2)	11	55
Wide (≥2)	9	45
Keratinized tissue phenotype		
Thick	20	100
Thin	0	0
Adjacent tooth		
Present	15	75
Absent	5	25
Implant position		
Anterior	0	0

Posterior	20	100
Implant diameter (mm)		
Small (<4)	6	30
Medium (4-<5)	13	65
Large (≥5)	1	5
Implant length (mm)		
Short (<8)	1	5
Medium (8-10)	12	60
Long (>10)	7	35
Implant design		
Bone level	20	100
Tissue level	0	0
Prosthesis		
Screw retained	1	5
Cement retained	15	75
Screw-and cement-retained	4	20

n - number of teeth

Table 2. Distribution of keratinized tissue around implant's contralateral tooth

Keratinized gingiva characteristics	*n*	Proportion (%)
Keratinized tissue width (mm)		
Narrow (<2)	2	10
Wide (≥2)	18	90
Keratinized tissue phenotype		
Thick	20	100
Thin	0	0

n - number of teeth

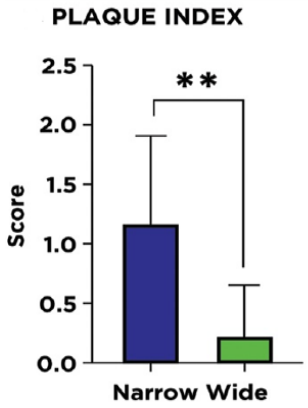
The mean distribution of the keratinized tissue width around the implant was half that of its contralateral tooth. The clinical mean parameter score showed that the soft tissue around the implant and its contralateral tooth was classified as mild inflammation **(Table 3)**.

Table 3. Mean distribution of keratinized tissue characteristics, clinical parameter scores and tumour necrosis factor-levels in implant and contralateral tooth

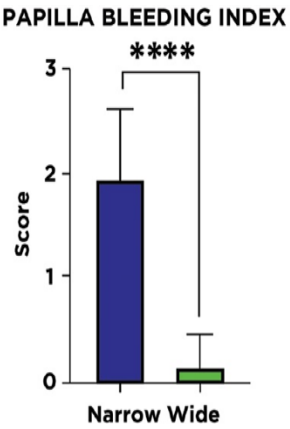
Keratinized tissue characteristics, clinical parameter scores, and TNF-α levels	Mean±SD	
	Implant (*n*=20)	Contralateral tooth (*n*=20)
Keratinized tissue width (mm)	1.67±1.26	3±1.01
PI	0.75±0.78	0.60±0.60
PBI	1.10±1.07	0.65±0.93
PD (mm)	2.65±0.99	2.25±0.78
TNF-α levels (ng/mL)	214.43±6.89	216.45±5.78

SD - Standard deviation; PI - Plaque index; PBI - Papilla bleeding index; PD - Pocket depth; TNF-α - Tumour necrosis factor-α; *n* - number of implants/teeth

A comparative analysis between the wide and narrow keratinized tissue groups around the implant showed a significant difference in PI ($P = 0.003$), PBI ($P = 0.000$), and PD ($P = 0.004$) but not in the TNF-α levels ($P = 0.606$) between the groups **(Figure 2)**. The comparison between the wide and narrow keratinized tissue groups around the tooth showed a significant difference in PI ($P = 0.020$) and PBI ($P = 0.027$) but not in PD ($P = 0.160$) and TNF-α ($P = 0.236$) **(Figure 3)**. No difference was found in the clinical parameter score and TNF-α levels between the groups of implants and their contralateral teeth in either wide or narrow keratinized tissue **(Table 4)**.



a)



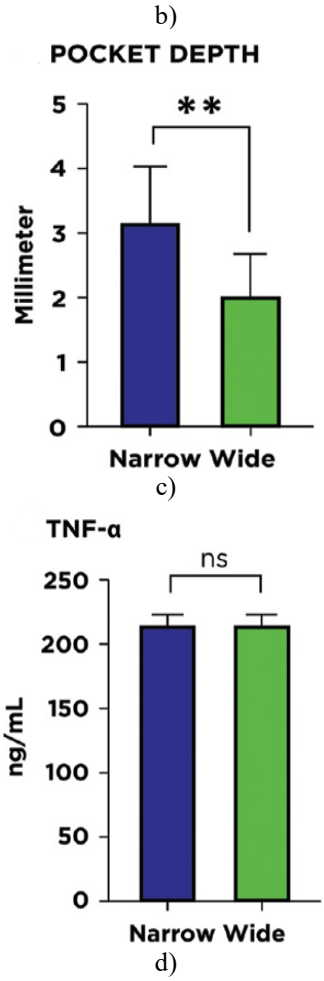
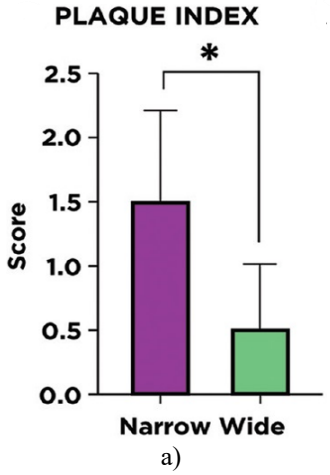


Figure 2. Clinical parameter scores and TNF-α Levels around implant. PI; PBI; PD; TNF-α; (a-d) PI, PBI, PD, and TNF-α levels between wide and narrow keratinized tissue around implant. NS $P \geq 0.05$, *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, ****$P < 0.0001$, by Independent *t*-test analysis. TNF-α – Tumour necrosis factor alpha, PI – Plaque index, PBI – Papilla bleeding index, PD – Pocket depth, NS – Nonsignificant



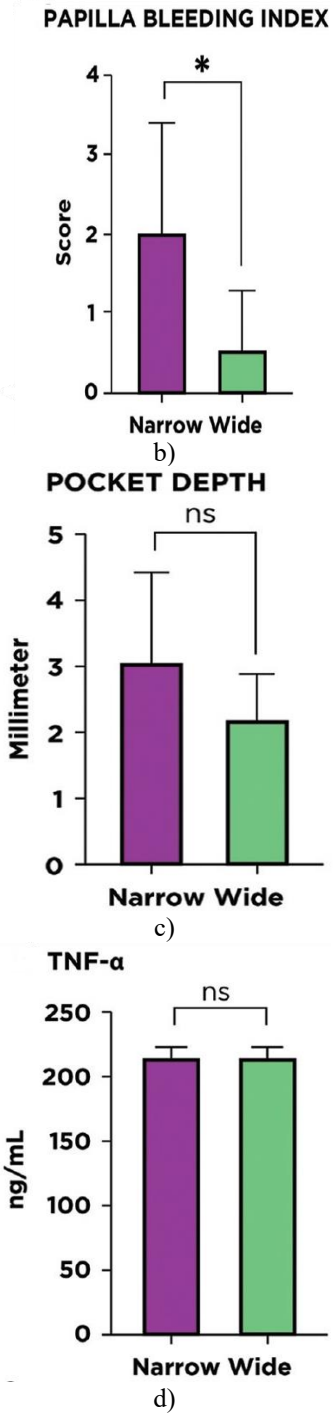


Figure 3. Clinical parameter scores and TNF-α levels around contralateral tooth. (a-d) TNF-α levels between wide and narrow keratinized tissue around contralateral tooth. ns $P \geq 0.05$, *$P < 0.05$, by independent *t*-test analysis. TNF-α – Tumor necrosis factor alpha, PI – Plaque index, PBI – Papilla bleeding index, PD – Pocket depth, ns – Nonsignificant

Table 4. Differences in clinical parameter scores and tumour necrosis factor-α levels between implant and contralateral tooth of wide and narrow keratinized tissue

Clinical parameter scores and TNF-α levels	Wide			Narrow		
	Implant	Contralateral tooth	*P*	Implant	Contralateral tooth	*P*
PI	0.22±0.44	0.58±0.61	0.128	1.18±0.75	1.50±0.71	0.591
PBI	0.11±0.33	0.53±0.77	0.137	1.91±0.70	2.00±1.41	0.884
PD	2.00±0.71	2.16±0.69	0.579	3.18±0.87	3.00±1.41	0.805
TNF-α levels	215.34±5.34	216.98±5.43	0.461	213.68±8.12	211.76±7.43	0.763

P<0.05=Significantly different (Independent *t*-test). PI - Plaque index; PBI - Papilla bleeding index; PD - Pocket depth; TNF-α - Tumour necrosis factor-α; *P* - probability/significant value

Table 5 presents Spearman's correlation analysis. Statistically significant correlations were found between the clinical parameter score and the keratinized tissue width of peri-implant tissue in PI ($r = -0.630$), PBI ($r = -0.881$), and PD ($r = -0.636$). The TNF-α levels revealed a very weak correlation with the keratinized tissue width of peri-implant tissue ($r = +0.166$).

Table 5. Correlation of keratinized tissue width around implant and contralateral tooth with clinical parameter scores and tumour necrosis factor-α levels

Clinical parameter scores and TNF-α levels	Keratinized tissue width			
	Implant		Contralateral tooth	
	r	*P*	*r*	*P*
PI	(−) 0.630	0.003*	(−) 0.440	0.052
PBI	(−) 0.881	0.000*	(−) 0.443	0.050
PD	(−) 0.636	0.003*	(−) 0.255	0.278
TNF-α levels	(+) 0.166	0.485	(+) 0.347	0.134

The value of **P*<0.05=Significantly different. Spearman's test (test two numeric-categorical unpaired groups). Value of *r* (−) opposite direction, (+) same direction. The value of *r*: 0-≤0.25 very weak, 0.26-≤0.5 medium, 0.51-≤0.75 strong, 0.76-≤1 very strong. PI - Plaque index; PBI - Papilla bleeding index; PD - Pocket depth; TNF-α - Tumour necrosis factor-α; *r* - Correlation coefficient; *P* - Probability/significant value

Peri-implant and periodontal soft tissue morphologies are similar in appearance and structure, and they are distinguished by their resistance to bacterial invasion [23, 25, 40–43]. Natural teeth have the periodontium as a healthy defense mechanism, which consists of the gingiva, epithelium sulcus, epithelial attachments, and connective tissue attachments. Free gingiva is the area where biofilm enters the crevicular area and stimulates the activation of neutrophils and lymphocytes, resulting in an inflammatory response [23, 44]. The complex gingival connective tissue fibers form bundles, and some enter the cementum, alveolar bone, and cementoenamel junction, acting as a protective mechanism.

Implants have less protection than natural teeth because implants are trans-tissue elements in which the abutments, implant neck, and restorations penetrate the tissue and adapt without entering the cementum. Supracrestal collagen fibers in the peri-implant are parallel to the axis of the implant axis with a circular shape, thus making their attachment more susceptible to inflammation [3, 18, 24, 25, 45, 46]. Peri-implant soft tissue is also important in maintaining esthetic function and masticatory pressure, but its ability to regenerate is restricted due to the limited number of cells and lack of vascularity [25, 47, 48].

Keratinized tissue includes free and attached gingiva from the gingival margin to the mucogingival junction [22, 36, 49]. Compared to the nonkeratinized tissue, this tissue is usually thicker, denser, and strongly attached to the underlying bone as a protective function between the oral environment and the underlying dental implant [50]. The width of the keratinized tissue is the most frequent characteristic studied for its effect on the peri-implant status associated with discomfort when brushing teeth [5]. The thickness of keratinized tissue, also known as the AAP 2017: periodontal phenotype, is often associated with bone loss if the thickness is inadequate [10, 21, 51–54].

Several clinical studies have reported high gingival bleeding index, PI, PD, attachment loss, and soft tissue recession in areas with narrow keratinized tissue (<2 mm), but others have reported that the width of the keratinized tissue did not affect the gingival index where bone loss occurs [3, 6, 8, 19, 23, 25, 38]. Lang and Löe demonstrated that healthy periodontal tissue requires a good soft tissue seal around the teeth and that dental implants require at least 2 mm of keratinized tissue with 1 mm of attachment [36]. The success of implant treatment is osseointegration, and the implant must be covered by tissue. The role of soft tissue in long-term implant maintenance is to prevent external pressure, risk of infection, and epithelial growth [35].

In this study, keratinized tissue around the implant and its contralateral tooth was measured to find the correlation of both tissues with the clinical parameter score and TNF-α levels. The data showed mean distribution of keratinized tissue width around the implant (1.67 [±1.26]) was half that

around its contralateral tooth (3 [±1.01]). Apart from peri-implant tissue characteristics, several other implant-related data were also collected, such as presence of neighboring teeth, implant position, implant diameter, implant length, implant design, and implant prosthesis. It was found that the entire implant position was in the posterior area and using a bone-level implant system. This proportion is good enough so that the study sample is uniform, as shown in **Tables 1 and 2**. The posterior area is reported to have a higher tendency for biological complications to occur [39].

Implant treatment fails when osseointegration is not maintained; this is usually caused by peri-implant diseases [4, 8, 9, 18, 21, 29, 55–59]. A meta-analysis reported that the prevalence of peri-implantitis was 22% (95% confidence interval: 14–30) [60]. Peri-implant disease is an inflammatory process caused by bacteria in the osseointegrated tissue around the implant [8, 9, 29, 40, 55, 61]. Peri-implant diseases are classified into two categories: peri-implant mucositis and peri-implantitis. Peri-implant mucositis is an inflammatory reaction of peri-implant soft tissue, i.e., reversible, whereas peri-implantitis involves hard tissue and is irreversible. Corrêa *et al*. found that the presence of periodontal pathogens is necessary but not sufficient for the initiation of peri-implantitis.

Studies have suggested that osteo-immunoinflammatory mediators (i.e., cytokines) play an important role in peri-implant tissue damage [62–64]. TNF-α is a pro-inflammatory cytokine involved in systemic and local inflammation through different signaling pathways. It induces the upregulation of adhesion molecules on leukocytes and endothelial cells, stimulates the production of chemokines that recruit leukocytes to areas of inflammation, and increases the production of collagenase and prostaglandin enzymes, thereby triggering collagen breakdown and bone resorption [63, 65]. The increase in plaque and bleeding in response to probing of the dental implants may be associated with a high risk of mucositis and peri-implantitis.

The success of implant treatment can be evaluated clinically, immunologically, microbiologically, and radiographically. Soft tissue evaluation is carried out after at least 3 months of implant functioning in the oral cavity [6, 8, 29, 66]. There are various ways to measure the thickness of keratinized tissue, including visual examination, placement of a periodontal probe in the sulcus, direct measurement using a needle, ultrasound, and three-dimensional radiographic examination [37]. Clinical parameters, such as PI, gingival bleeding, PD, recession, and level of attachment, are commonly used to detect inflammation in peri-implant soft tissue [7, 8, 21]. The mean scores of clinical parameters such as PI and PD were relatively the same between the implants and the contralateral teeth, except that the PBI in the implants was almost twice that of the contralateral teeth. However, in terms of clinical parameter scores obtained, both soft tissue around the implant and the contralateral tooth have mild inflammation, as shown in **Table 3**.

Immunological evaluation in the form of TNF-α is the highest in participants with peri-implant tissue inflammation [9, 40, 55]. Recent studies have demonstrated the use of peri-implant crevicular fluid (PICF) as a good diagnostic tool for detecting the early pathological stages of peri-implant disease [39]. Both PISF and GCF originate from the vessels of the tissue plexus around the implant and the contralateral tooth. These fluids accommodate molecules whose levels may reflect both local and systemic inflammation [67]. Belibasakis reported higher concentrations of TNF-α, interleukin-17, Interleukin-1b, and nitric oxide in the PICF of patients with peri-implantitis [29]. Conversely, this study found no difference in the TNF-α level between the groups of wide and narrow keratinized tissue around the implant. One possible reason for TNF-α being not significant is that the clinical parameter scores of PI (0.75), PBI (1.1), and PD (2.65) were still categorized as mild inflammation, thus causing the low expression of TNF-α.

The necessity of keratinized tissue around implants has been extensively debated and is of concern. Many studies have reported differing results regarding the link between the two, but the extent of the correlation between them has yet to be ascertained. The presence of keratinized tissue around an implant is considered to provide a comfortable environment for daily oral cleaning [5, 21]. Techniques such as free gingival palatal grafts have been performed to correct the inadequate condition of keratinized tissue. Further research with more subjects and long-term evaluations is suggested to confirm the role of keratinized tissue in implant maintenance. Impaired oral hygiene is responsible for the manifestation of tissue inflammation around the implant in narrow keratinized tissue.

This study showed that the clinical parameter score was statistically different between the groups of wide and narrow keratinized tissue around the implant with PI ($P = 0.003$) and PBI ($P = 0.000$) but not in PD ($P = 0.004$) and TNF-α ($P = 0.606$). Then, a comparison between the groups of wide and narrow keratinized tissue around the tooth also showed significant differences in PI ($P = 0.020$) and PBI ($P = 0.027$) but not in PD ($P = 0.160$) and TNF-α ($P = 0.276$). Even though the soft tissue around natural teeth, which acts as a protective mechanism, is strong, it still tends to increase the clinical parameter score if the keratinized tissue width is inadequate. Spearman correlation analysis revealed a statistically significant correlation between each clinical parameter score and keratinized tissue width of peri-implant tissue with coefficients of PI ($r = -0.630$), PBI ($r = -0.881$), and PD ($r = -0.636$). This result indicates the importance of keratinized tissue around the implant to maintain gingival health and prevent peri-implant disease [18, 39].

Conclusion

The keratinized tissue width around implants showed a strong correlation with PI, PBI, and PD. This finding is important in maintaining implant integrity for long-term implant stability. The immunological parameter found no difference in the TNF-α levels between the groups of wide and narrow keratinized tissue around the implant. This shows the importance of adequate keratinized tissue around an implant to maintain implant integrity.

Acknowledgments: This study was performed at Dental Teaching Hospital, Faculty of Dentistry, Universitas Indonesia. Implant brands used in this study were Straumann, C-Tech, and Dentium. However, the dental implant manufactures have no intervention to the result of this study. This publication's contents are completely the responsibility of the authors and do not necessarily represent the official views of the Universitas Indonesia. Authors report no conflict of interest regarding this study.

Conflict of interest: None

Financial support: Grant from HIBAH PUTI Universitas Indonesia 2020 (NKB-4806/UN2.RST/HKP. 05.00/2020).

Ethics statement: None

References

1. 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):E214.
2. Frisch E, Wild V, Ratka-Krüger P, Vach K, Sennhenn-Kirchner S. Long-term results of implants and implant-supported prostheses under systematic supportive implant therapy: a retrospective 25-year study. Clin Implant Dent Relat Res. 2020;22(4):689-96.
3. Gobbato L, Avila-Ortiz G, Sohrabi K, Wang CW, Karimbux N. The effect of keratinized mucosa width on peri-implant health: a systematic review. Int J Oral Maxillofac Implants. 2013;28(6):1536-45.
4. Papaspyridakos P, Chen CJ, Singh M, Weber HP, Gallucci GO. Success criteria in implant dentistry: a systematic review. J Dent Res. 2012;91(3):242-8.
5. Souza AB, Tormena M, Matarazzo F, Araújo MG. The influence of peri-implant keratinized mucosa on brushing discomfort and peri-implant tissue health. Clin Oral Implants Res. 2016;27(6):650-5.
6. de Araújo MF, Filho AF, da Silva GP, de Melo ML, Napimoga MH, Rodrigues DB, et al. Evaluation of peri-implant mucosa: clinical, histopathological and immunological aspects. Arch Oral Biol. 2014;59(5):470-8.
7. Klinge B, Klinge A, Bertl K, Stavropoulos A. Peri-implant diseases. Eur J Oral Sci. 2018;126 Suppl 1:88-94.
8. Ata-Ali J, Flichy-Fernández AJ, Alegre-Domingo T, Ata-Ali F, Palacio J, Peñarrocha-Diago M. 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.
9. Máximo MB, de Mendonça AC, Santos VR, Figueiredo LC, Feres M, Duarte PM. Short-term clinical and microbiological evaluations of peri-implant diseases before and after mechanical anti-infective therapies. Clin Oral Implants Res. 2009;20(1):99-108.
10. Doornewaard R, Jacquet W, Cosyn J, De Bruyn H. How do peri-implant biologic parameters correspond with implant survival and peri-implantitis? A critical review. Clin Oral Implants Res. 2018;29 Suppl 18:100-23.
11. Bate GB, Adeleye AO, Ijanu EM, Olalere EO, Amoo AO, Asaju CI, et al. Quality assessment of wastewater: physicochemical and bacteriological evidence from dutse abattoir, North-West Nigeria. World J Environ Biosci. 2023;12(3):58-66. doi:10.51847/5xxrD8Fbka
12. Nagdalian A, Askerova A, Blinov A, Shariati MA. Evaluation of the toxicity of copper oxide nanoparticles toward pea seeds. World J Environ Biosci. 2024;13(3):23-30. doi:10.51847/A2gMbUMBUD
13. Mehrzad K, Yazdanpanah F, Arab M, Ghasemi M, Radfar A. Relationship between stress, anxiety, and depression with happiness in students of Bam medical university in 2019. J Adv Pharm Educ Res. 2022;12(2):51-6. doi:10.51847/dJZ1dCmMK6
14. Sakhnenkova TI, Abdul-Kadyrova LR, Akhilgova ZA, Brovikova AA, Markov OO, Saribekyan AA, et al. Morphological and biochemical analysis of 3D scaffold based on biocompatible polymer for tissue engineering. J Adv Pharm Educ Res. 2023;13(3):29-33. doi:10.51847/v8o0GbXJdN
15. Huyen NT, Nghi PH, Phuong ĐTL, Trang TTT, Huyen LT. Public debt and prosperity nexus in asian countries: nonlinearity and threshold analysis. J Organ Behav Res. 2023;8(1):74-91. doi:10.51847/tw5g65dco8
16. Shoghi B, Kian H. The role of managers in developing creativity and managing talent. J Organ Behav Res. 2022;7(2):18-29. doi:10.51847/uy31rvfml2
17. Petronis Z, Pliatkute I, Janovskiene A, Leketas M. The relationship between cervical spine abnormalities and temporomandibular joint internal disorders: a systematic review of literature. Ann Dent Spec. 2023;11(4):20-8. doi:10.51847/sGUN5P9OQA
18. Adibrad M, Shahabuei M, Sahabi M. Significance of the width of keratinized mucosa on the health status of the supporting tissue around implants supporting overdentures. J Oral Implantol. 2009;35(5):232-7.
19. Buyukozdemir Askin S, Berker E, Akincibay H, Uysal S, Erman B, Tezcan İ, et al. Necessity of keratinized tissues for dental implants: a clinical, immunological,

and radiographic study. Clin Implant Dent Relat Res. 2015;17(1):1-12.
20. Zigdon H, Machtei EE. The dimensions of keratinized mucosa around implants affect clinical and immunological parameters. Clin Oral Implants Res. 2008;19(4):387-92.
21. Chiu YW, Lee SY, Lin YC, Lai YL. Significance of the width of keratinized mucosa on peri-implant health. J Chin Med Assoc. 2015;78(6):389-94.
22. Greenstein G, Cavallaro J. The clinical significance of keratinized gingiva around dental implants. Compend Contin Educ Dent. 2011;32(7):24-31.
23. Monje A, Blasi G. Significance of keratinized mucosa/gingiva on peri-implant and adjacent periodontal conditions in erratic maintenance compliers. J Periodontol. 2019;90(5):445-53.
24. Kelekis-Cholakis A. The importance of keratinized tissue around implants there is controversy in the literature as to whether augmentation of soft tissue around dental implants should be performed to obtain an added band of keratinized tissue. J Cosmet Dent. 2015;31(3):119-24.
25. Bouri A Jr, Bissada N, Al-Zahrani MS, Faddoul F, Nouneh I. Width of keratinized gingiva and the health status of the supporting tissues around dental implants. Int J Oral Maxillofac Implants. 2008;23(2):323-6.
26. Cantile T, Lombardi S, Quaraniello M, Riccitiello F, Leuci S, Riccitiello A. Studying the knowledge and behavior of parents in dealing with children's dental injuries. Ann Dent Spec. 2024;12(2):1-5. doi:10.51847/FYF9lXJwPt
27. Kartashev VP, Xingyuan S, Medvedev IN, Tkacheva ES, Vorobyeva NV. Physiological changes in the erythrocytes of an aging organism experiencing physical. J Biochem Technol. 2023;14(1):50-6. doi:10.51847/GGLSMMHC5s
28. Ouafa B, Ifriqya M, Ikram T. Evaluation of biological activities of chamaeleo chamaeleon: a reptile used in traditional folk medicine in Algeria. J Biochem Technol. 2022;13(4):15-9. doi:10.51847/eD9GJaf2j7
29. Belibasakis GN. Microbiological and immuno-pathological aspects of peri-implant diseases. Arch Oral Biol. 2014;59(1):66-72.
30. Efremov A. Relieving psychosomatic pain and negative emotions through dehypnosis. Asian J Indiv Organ Behav. 2023;3:18-24. doi:10.51847/BPFsWgpeFd
31. Duarte PM, de Mendonça AC, Máximo MB, Santos VR, Bastos MF, Nociti FH. Effect of anti-infective mechanical therapy on clinical parameters and cytokine levels in human peri-implant diseases. J Periodontol. 2009;80(2):234-43.
32. Ghassib I, Chen Z, Zhu J, Wang HL. Use of IL-1β, IL-6, TNF-α, and MMP-8 biomarkers to distinguish peri-implant diseases: a systematic review and meta-analysis. Clin Implant Dent Relat Res. 2019;21(1):190-207.
33. Faot F, Nascimento GG, Bielemann AM, Campão TD, Leite FR, 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.
34. Zani SR, Moss K, Shibli JA, Teixeira ER, de Oliveira Mairink R, Onuma T, et al. Peri-implant crevicular fluid biomarkers as discriminants of peri-implant health and disease. J Clin Periodontol. 2016;43(10):825-32.
35. Kim BS, Kim YK, Yun PY, Yi YJ, Lee HJ, Kim SG, et al. Evaluation of peri-implant tissue response according to the presence of keratinized mucosa. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;107(2):e24-8.
36. Lang NP, Löe H. The relationship between the width of keratinized gingiva and gingival health. J Periodontol. 1972;43(10):623-7.
37. Aguilar-Duran L, Mir-Mari J, Figueiredo R, Valmaseda-Castellón E. Is measurement of the gingival biotype reliable? Agreement among different assessment methods. Med Oral Patol Oral Cir Bucal. 2020;25(1):e144-9.
38. Boynueğri D, Nemli SK, Kasko YA. Significance of keratinized mucosa around dental implants: a prospective comparative study. Clin Oral Implants Res. 2013;24(8):928-33.
39. 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(2):264-72.
40. Ferreira SB Jr, Figueiredo CM, Almeida AL, Assis GF, Dionísio TJ, Santos CF. Clinical, histological, and microbiological findings in peri-implant disease: a pilot study. Implant Dent. 2009;18(4):334-44.
41. Berglundh T, Abrahamsson I, Welander M, Lang NP, Lindhe J. Morphogenesis of the peri-implant mucosa: an experimental study in dogs. Clin Oral Implants Res. 2007;18(1):1-8.
42. Schupbach P, Glauser R. The defense architecture of the human periimplant mucosa: a histological study. J Prosthet Dent. 2007;97(1 Suppl):S15-25.
43. Fitero A, Negruț N, Cseppento DCN, MirelaTit D, Negru PA, Bustea C, et al. Inequities in antiviral therapy for diabetic individuals affected by COVID-19. Ann Pharm Pract Pharmacother. 2023;3:9-20. doi:10.51847/BAIbQWifek
44. Xie B, Liu Y, Li X, Yang P, He W. Enhancing the dissolution rate of dolutegravir sodium using nanosuspension technology and a 32 factorial design. Pharm Sci Drug Des. 2023;3:12-9. doi:10.51847/2uCOYf3jPn
45. Danchin A, Ng TW, Turinici G. Transmission pathways and mitigation strategies for COVID-19. Interdiscip Res Med Sci Spec. 2024;4(1):1-10. doi:10.51847/p0YhQPxvkW

46. Balaji A, Jei JB, Murugesan K, Muthukumar B. Case report on distal extension edentulous rehabilitation using claspless extra-coronal attachments. J Curr Res Oral Surg. 2022;2:16-9. doi:10.51847/OhXCPOyjBp
47. Subramanian S, Anbarasu P, Nallusamy A, Ramesh B. An in vitro evaluation of the effectiveness of four remineralizing agents. Turk J Dent Hyg. 2022;2:18-25. doi:10.51847/3lmv1TQOcM
48. Silva-Hormazábal M, Alsina Á. Exploring the impact of integrated education on medical sciences: a comprehensive review. Ann Pharm Educ Saf Public Health Advocacy. 2023;3:30-6. doi:10.51847/h9MdCIGsUf
49. Guo L, He Y, Sun Y, Chan JSM, You J, Jia L, et al. Longitudinal study on the characteristics of traditional chinese medicine (TCM) constitutions and related influencing factors in women in Hong Kong. J Med Sci Interdiscip Res. 2022;2(1):23-35. doi:10.51847/B0MHcO112v
50. Lang NP, Bartold PM. Periodontal health. J Periodontol. 2018;89 Suppl 1:S9-16.
51. Puisys A, Linkevicius T. The influence of mucosal tissue thickening on crestal bone stability around bone-level implants. A prospective controlled clinical trial. Clin Oral Implants Res. 2015;26(1):123-9.
52. Koh RU, Oh TJ, Rudek I, Neiva GF, Misch CE, Rothman ED, et al. Hard and soft tissue changes after crestal and subcrestal immediate implant placement. J Periodontol. 2011;82(8):1112-20.
53. Linkevicius T, Apse P, Grybauskas S, Puisys A. The influence of soft tissue thickness on crestal bone changes around implants: a 1-year prospective controlled clinical trial. Int J Oral Maxillofac Implants. 2009;24(4):712-9.
54. Avila-Ortiz G, Gonzalez-Martin O, Couso-Queiruga E, Wang HL. The peri-implant phenotype. J Periodontol. 2020;91(3):283-8.
55. Charalampakis G, Leonhardt Å, Rabe P, Dahlén G. Clinical and microbiological characteristics of peri-implantitis cases: a retrospective multicentre study. Clin Oral Implants Res. 2012;23(9):1045-54.
56. Dwingadi E, Soeroso Y, Lessang R, Priaminiarti M. Evaluation of alveolar bone on dental implant treatment using cone beam computed tomography. Pesqui Bras Odontopediatr Clin Integr. 2019;19:e0047.
57. Salvi GE, Lang NP. Diagnostic parameters for monitoring peri-implant conditions. Int J Oral Maxillofac Implants. 2004;19 Suppl:116-27.
58. Enersen M. Risk factors for periodontal disease. Oral Infect Cardiovasc Dis. 2011;62:17-25.
59. Sayuti E, Thahar B, Soemantri ES, Rasyid HN. Microbiological evaluation of dental implants using quantification of porphyromonas gingivalis in dental teaching hospital universitas Indonesia from 2009-2014. J Int Dent Med Res. 2018;11(6):1636-9.
60. Derks J, Tomasi C. Peri-implant health and disease. A systematic review of current epidemiology. J Clin Periodontol. 2015;42 Suppl 16:S158-71.
61. Berglundh T, Armitage G, Araujo MG, Avila-Ortiz G, Blanco J, Camargo PM, et al. Peri-implant diseases and conditions: consensus report of workgroup 4 of the 2017 world workshop on the classification of periodontal and peri-implant diseases and conditions. J Clin Periodontol. 2018;45 Suppl 20:S286-91.
62. Graves D. Cytokines that promote periodontal tissue destruction. J Periodontol. 2008;79(8):1585-91.
63. Gomes FI, Aragão MG, Barbosa FC, Bezerra MM, de Paulo Teixeira Pinto V, Chaves HV. Inflammatory cytokines interleukin-1β and tumour necrosis factor-α – Novel biomarkers for the detection of periodontal diseases: a literature review. J Oral Maxillofac Res. 2016;7(2):e2.
64. Corrêa MG, Pimentel SP, Ribeiro FV, Cirano FR, Casati MZ. Host response and peri-implantitis. Braz Oral Res. 2019;33:e066.
65. Noh MK, Jung M, Kim SH, Lee SR, Park KH, Kim DH, et al. Assessment of IL-6, IL-8 and TNF-α levels in the gingival tissue of patients with periodontitis. Exp Ther Med. 2013;6(3):847-51.
66. Hämmerle CH, Giannobile WV; Working Group 1 of the European Workshop on Periodontology. Biology of soft tissue wound healing and regeneration – Consensus report of Group 1 of the 10th European Workshop on Periodontology. J Clin Periodontol. 2014;41 Suppl 15:S1-5.
67. Buduneli N, Kinane DF. Host-derived diagnostic markers related to soft tissue destruction and bone degradation in periodontitis. J Clin Periodontol 2011;38 Suppl 11:85–105.