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PERI-IMPLANTITIS A POSSIBLE RISK BY BACTERIAL COLONIZATION AT THE IMPLANT-ABUTMENT INTERFACE: A SYSTEMIC REVIEW AND META-ANALYSIS

Yash Desai*[1], Amit Benjamin[1,2], Saba Supariwala[1] and Samruddhi Kadaki[3]

[1]Private Practice, Mumbai, Maharashtra, India.
[2]Department of Periodontics, Y.M.T Dental College and Hospital, Kharghar, Navi Mumbai, Maharashtra, India.
[3]D.Y. Patil University, School of Dentistry, Nerul, Navi Mumbai, Maharashtra, India.

***Corresponding Author: Yash Desai**
Private Practice, Mumbai, Maharashtra, India.

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ABSTRACT

Purpose: The purpose of this systemic review and meta-analysis was to estimate the colony of microorganisms on bone-level implants at the implant-abutment interface (IAI) and to find its similarity with peri-implant conditions. **Study selection:** The study was emphasized for implants in function for at least 1 year, whether the two-piece osseointegrated implants, associate to rise in the number of bacterial colonization and the outcome of peri-implantitis, in comparison to healthy peri-implant condition. Using a mixture of MeSH (Medical Subject Headings) and search terms the Search strategy circumscribes the on-line (MedLine, Google Scholar, Cochrane library) literature from 1990 till March 2015 which was published in English. According to the ARRIVE and CONSORT statement guidelines, quality assessment of carefully chosen full-text articles was achieved. The total bacterial count was calculated and equated to IAI with or without peri-implant pathology for Porphyromonas gingivalis, Fusobacterium nucleatum, Treponema denticola, Tannerella forsythia, and Prevotella intermedia. **Results:** The inclusion principles and quality assessment were fulfilled from a total of 14 articles, and 1029 implants record. According to the studies patients with the two-piece implant system displayed the contamination of IAI. A substantial difference in total bacterial count between implants affected by peri-implantitis versus healthy peri-implant tissues (0.3870.055; 95% CI 0.279–0.496) were indicated by meta-analysis. However, except for T. forsythia, less bacterial colonization was noticed in the healthy IAI for all the examined gram-negative bacteria. **Conclusions:** An increase in bacterial colonization with peri-implantitis in comparison to those present in healthy peri-implant tissues was substantially reported for periodontal pathogenic bacteria in the IAI patients.

KEYWORDS: Dental implant, Implant-abutment interface (IAI), Bacterial colonization, peri-implantitis.

1. INTRODUCTION

Dental implants are widely used to restore the edentulous area. Implant rehabilitation is successful with adequate bone support around the implant fixture. Lee. et al indicated that prosthetic loading or bacterial infection could be related to implant failure and they reported that the prevalence of mucositis is 29.48% and that of peri-implantitis is 9.25%. However, osseointegration can be affected by the oral condition, in particular, micro-leakage at the implant-abutment interface (IAI) representing the site for dental plaque aggregation favoring bacterial leakage, which can upsurge the number of inflammatory cells at the level of the peri-implant sulcus IAC[1,2], causing peri-implantitis. The two-piece implants present a micro-leakage between the implants and the abutment. These spaces may present a bacterial reservoir that could contaminate the implants interface once early colonized with the peri-implant tissues.

The presence of micro-leakage and accumulation of bacteria in close relation to the bone may also lead to bone loss.[8,12] During the first year after implant placement the major part of the marginal bone loss was recorded after which an adequate level of bone stabilized over the years. The micro-leakage at the junction permits passage of acids, enzymes, bacteria, and their metabolic products which affects the periodontal tissue leading to bleeding on probing, redness, swelling, and odor. Bacteria found at the level of IAI can be either with or without anaerobic or facultative anaerobic microbes. It depends on the features of the microhabitat. Patients with periodontal conditions are at more risk of having peri-implantitis.

A current review of literature stated that Porphyromonas gingivalis, Tannerella forsythia, and Treponema denticola were found in subgingival biofilm samples. Observational studies have indicated that peri-implantitis were more associated with opportunistic pathogens such as pseudomonas aeruginosa and staphylococcus Aureus,

Fungal organism such as candida albicans, candida boidinii, Penicillium, rhadotorula Laynges, paelicomyces spp. and viruses such as human cytomegalovirus, Epstein bar virus. The purpose of this systemic review and meta-analysis was to estimate the colony of micro-organisms on bone level implants, at the implant-abutment interface on a two-piece, independently from the configuration of the linking, and examine if it narrates to the onset of peri-implantitis.

2. Study selection

The following estimation gave the conformation of the reports for Systematic Reviews and Meta-Analysis (PRISMA) tips (https://www.prisma-statement.org).[15] The protocol to be followed for this systematic review is out there among the international prospective register of systematic reviews (PROSPERO, https://www.crd.york.ac.uk/PROSPERO/) in conjunction with identification number CRD42016037481. The engrossed question of the review was to identify if there is a correlation between the presence of higher microbial count and the onset of peri-implantitis, in context to healthy peri-implant tissues in patients with the two-piece osseointegrated implants. Peri-implantitis is described by the presence of peri-implant depth ≥ 5mm leading to hemorrhage while bleeding on probing or by suppuration, and radiographs of bone loss ≥ 3mm, compared to primary radiographs of the prosthetic restorations.

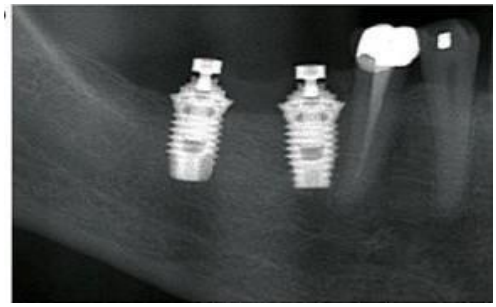


Fig. 1: Before peri-implantitis resembling implant.

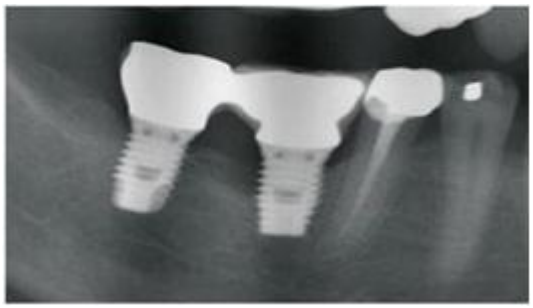


Fig. 2: After peri-implantitis. abutment interface.

2.1. Data sources

Articles which were published in English were only found with the data having the colonies of microorganisms at the IAI and its onset of peri-implantitis, were taken from 1990 till March 2015 PubMed information of the USA National Library of medication (https://www.ncbi.nlm.nih.gov/pubmed/), Google Scholar (https://www.google.com) and jointly the Cochrane Library (https://network.cochranelibrary.com/). Moreover, many other articles were searched manually to have it as a reference article.

2.2. Search strategy

At first, PICOS question ((P) Population, (I) Intervention, (C) Comparison between the implants, (O) Outcomes (S) Study design and its type) defined the search strategy, where P=The two-piece osseo-integrated implants with an analysis of peri-implantitis once in at least a year of function; I=Microbial organization at the IAI; C=Fit peri-implant environments; O=Survival percentage; S=Randomized skillful clinical trials (RCT) and clinical follow-up studies. The electronic databases were investigated with a mixture of MeSH (Medical Subject Headings) terms, search terms and their groupings: "the presence of bacterium" OR "microbiological findings"

2.3. Selection of study and its eligibility criteria

The abstracts and titles of all the articles were examined for the following criteria: (1) Articles should be written in English; (2) clinical examination of the patient study should be done; (3) studies should investigate the counts of various microbial species (bacterial count) at the IAI level in patients; (4) Randomized clinical trials (RCTs), forthcoming cohort studies or cross-sectional studies should be reviewed on implants for a minimum of 1 year.

After reviewing the complete text of the articles in context to the mentioned-above exclusion criteria, articles with the general characteristics, where there is no language limit, were not thought to be suitable:(a) Letters, narrative or historical assessments; (b) animal and in vitro studies; (c) Reports on domestically or negotiated sites and/or conditions (i.e. major bone defect previously implantation, bone pathologies, head and neck irradiation, treatment with bisphosphonates); (d) reports on patients without mechanical operation in the past 3 months or antibiotics at intermissions the latter six months before analysis.

2.4. Data assortment technique

Two prestige reviewers (M.C. and L.C.) searched and gathered the report from profound papers onto structured tables. Cohen's kappa values between examiners were designed at each primary and secondary position of the analysis. Discrepancies were resolved and a 3rd examiner (M.T.) was consulted.

Table 1: quality of all chosen full-text articles (Graziani et al. [19]; Pjetursson et al. [20]).

1st author	Ethical committee	Study selection	Standardization	Blinded assessor	Eligibility criteria	Connection	Total bacterial count methods	Participants	Number of implants	Risk of Bias
JervøeStorm et al.[27]	Yes	Prospective	Yes	Yes	Yes	Internal hex	Quantitative real-time PCR	66	26	Low
Persson et al.[30]	–	Cross-sectional	–	–	–	External hex	Colony morphology on the blood agar plates	10	28	High
Canulloe tal.[5]	Yes Yes	Cross-sectional Randomized controlled trial	Not clear Not clear	– –	Yes Yes	Different types (3) External hex	Quantitative real-time PCR DNA Extraction and Polymerase Chain Reaction (PCR) Amplifications	53 30	231 30	Moderate Moderate
Rimondi nietal.[26]	–	Prospective	–	–	–	Not reported	Scanning electron microscopy and energy dispersive x-ray spectroscopy (EDS) analysis.	17	17	High
Scarano et al.[31]	–	Cross-sectional	–	–	–	Different type (5)	Observed in normal reflecting light under a Laborlux-S light microscope	–	272	High
Quiryne n et al.[28]	–	Cross-sectional	–	–	Yes	External hex	Different phase contrast microscopy (DPCM)	9	18	High
Cosyn et al.[32]	Yes	Cross-sectional	Yes	–	–	External hex	DNA-DNA hybridization technique	8	58	Moderate
Canullo et al.[35]	Yes	Cross-sectional	Not clear	–	Yes	Not reported	Quantitative real-time PCR	38	52	Moderate
Canullo et al.[33]	–	Cross-sectional	Not clear	–	Yes	Different types (4)	Quantitative real-time PCR	40	60	Moderate
Penarro cha- Oltra et al.[33]	–	Cross-sectional	Not clear	–	Yes	Not reported	Quantitative real-time PCR	20	43	Moderate
Canulloe tal.[7]	Yes	Cross-sectional	Not clear	–	Yes	Not reported	Quantitative real-time PCR	110	225	Moderate
Rismanc hian et al.[25]	–	Randomized controlled trial	–	–	–	Different types (4)	TSB culture and SEM	–	36	High
Keller et al.[29]	–	Cross-sectional	–	–	Yes	Internal Morse taper	Darkfield microscope	30	30	High

2.5. Assessment of quality, dissimilarity, and risk of bias of individual studies

The risk of bias was examined by the reviewers at intervals according to the foundations provided by the CONSORT statement for the analysis of irregular controlled trials https://www.consort-statement.org), the instrument statement for empirical studies (https://www.strobe-statement.org), at the aspect of the changed matters from the Cochrane Collaboration Tool for assessing the risk of bias (Table 1).[19,20]

The quality valuation was achieved in 2 completely different stages, specifically clinical phase I where quality valuation was supported on full-text articles performed by several reviewers and in clinical phase II where disagreements were resolved upon discussion. Once grouping the scores at the trial of quality assessment, a general estimation of plausible risk of bias (low, moderate, or high) was completed for every chosen study. However, when all the factors were met a low risk of bias was evaluated when all the factors were partly met a moderate risk of bias was evaluated and when all the factors weren't met a high risk of bias was estimated (Cochrane reference for Systematic Reviews of Interventions, version. https://www. cochrane.org/ resources/handbook).

2.6. Measures and analysis of results

Descriptive statistics, meta-regression, and meta-analysis were achieved, on the premise of the comparable studies and identical reports. The microbiota existing at the IAI of implants operating for a minimum of 1 year was thought-about for information analysis. Bacteria's of the gram-negative organisms with (P. gingivalis, T. forsythia, T. denticola, P. intermedia, and Fusobacterium nucleatum) were removed and written as primary outcome variables.[21] The microbiota which is included for the analysis are usually detected at peri-implantitis sites and are found to upsurge the risk for peri-implant bone loss and health problem progression.[21–23] Mean variations were combined based on random-effects models. The variation between the studies, subgroup analysis, meta-analysis, and forest plots was planned to employ a coding program (Comprehensive MetaAnalysis V3; Biostat, Englewood, NJ, USA).

3. RESULTS

3.1. Study design

A total of 550 similar titles and abstracts were found during the electronic and manual research. Throughout the primary phase of design, 315 articles were excluded based on the titles and abstracts (k=0.72). However, in the secondary phase, complete full-text articles of the remaining 235 publications were evaluated and 198 articles were excluded since they didn't fulfill the inclusion criteria (k=0.98). Finally, a complete of 14 articles, reporting information from 1029 implants, were rigorously chosen that consummated inclusion criteria and quality assessment needed for the organized review (Fig. 1).

3.2. Study features

The 14 chosen articles were printed between 1993 and March of 2015, 2 of that were RCTs,[24,25] 2 prospective cohort studies.[26,27] and 6 cross-sectional studies.[5,7,28–35] However, only 1 prospective clinical study was written following the strobe light report for experimental studies (https://www. strobe-statement.org).[27] Hence, an accurate comparison between the articles chosen could not be possible.

3.3. Risk of bias during studies

All the requisites were not achieved by the retrospectives. One publication was associated with a little risk of bias.[27] seven with a moderate risk of bias.[5,7,24,32–35] and six with a high risk of bias.[8,25,26,29–31] The included articles received the least grading when evaluating submission to ethical committees (6/14), presence of blinded assessors (2/ 14), standardized procedures (1/14), and presence of eligible criteria (9/14) (Table 1).

3.4. Measures and meta-regression analysis

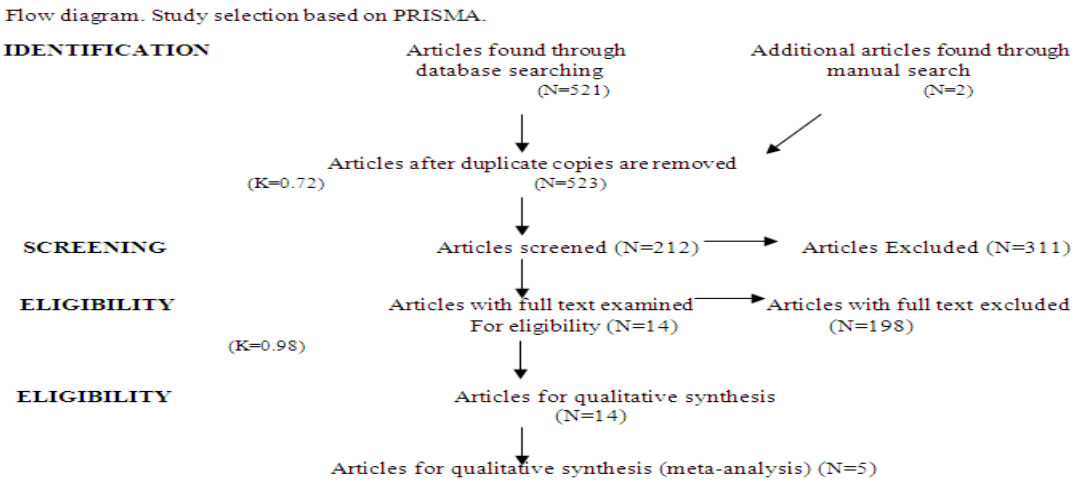
3.4.1. Bacterial leakage at the IAI

All the carefully chosen studies stated contamination of the IAI and the abutment surface in patients getting the assembly of a 2 stage implant system. Quantitative real-time polymerase chain reaction (PCR) was carried out for bacteria's in seven out of the fourteen studies.[5,7,24,27,33–35] where the succeeding pathogens were analyzed: P. gingivalis, Aggregatibacter actinomycetemcomitans, T. denticola, T. forsythia, Parvimonas Micra, P.intermedia, C.rectus, F.nucleatum, Candida albicans, Eikenella corrodens, Porphyromonas aeruginosa, and Enterococcus faecalis. While in one study the checkerboard DNA-DNA hybridization method was used,[32] in the other 6 studies distinct methods including a scanning electron microscopy were used to screen the colony morphology.[8,25,26,29– 31] In a study,[27] advanced colonies by periodontal pathogenic bacteria were well-defined in the internal parts of 2-piece implants. In the other study, intra-coronal components of screw-retained immobile restorations were highly contaminated in all the specimens.[32] Contamination of abutment screws are most likely to occur from the peri-implant sulcus concluded the IAI and abutment-prosthesis interface. Similarly, at the interior and exterior implant components between healthy peri-implant sulci and implants negotiated with peri-implantitis a significant difference in antibiotic-resistant nosocomial bacteria (E. faecalis and P. aeruginosa) were noticed.[35] Regarding the absence/presence of the bacterium analysis, none of the variations were found accurate between the study at the peri-implant fissure and the junctions within the abutments surfaces.[5] The composition of the microorganism at the adjacent teeth was the same as those found within the peri-implant fissure with a quite high frequency for P. gingivalis, T. forsythia, P. intermedia, P. Micra and E. corrodens.[5]

Two comparative studies between the healthy peri-implant condition in comparison to implants greatly stricken by peri-implantitis,[5,7] recorded microorganism contamination in each of the groups. Orange advanced species (P. intermedia, P. micra, F. nucleatum) were the predominant sites analyzed for each group.[36,37]

3.4.2. Bacterial leakage at the IAI concerning abutment linking design

Regarding the type of IAI the selected sample displayed greater differences. Four studies used numerous IAI styles.[5,25,31,34] whereas the other four manuscripts weren't reported within the type of IAI.[7,26,33,35] The analyzed connections showed contamination post five years of functional loading during the estimation of 4 IAIs.[34] In general, the implant connections showed qualitative and quantitative levels of inclination due to microbial colonization. Likewise, the mean micro-leakage size within the first 5hrs of loading showed a significant difference with various types of abutments.[25] However, at 24hr, 48hr, and 14days no significant effect of micro-leakage was found on microbial levels. Thus, the usage of standard abutments significantly reduced the microgap size in comparison to the customized ones. The study determined the analyzed abutments were comparable for all of the micro-leakage in the connection area.



3.4.3. Meta-regression and analysis of subgroups

Five studies, with a total of 620 implants (n=223 with peri-implantitis; n=399 with healthy peri-implant conditions) in function for at least 1year, were included in the meta-analysis.[5,7,27,33,34] Gram-negative anaerobic bacteria showed resemblance to chronic periodontitis and resulted to upsurge the risk for peri-implant bone loss and progression of disease due to the presence of odontogeenic pathogens (P. gingivalis, T. forsythia, T. denticola, P. intermedia, F. nucleatum) (Table 2).[10,21–23] Thus, the mean differences in bacteria were statistically substantial between the two analyzed groups, with higher values in implants with peri-implantitis (difference: 0.387 0.055; 95% CI 0.279–0.496, p=0.000).

Table 2: Reports studies of gram-negative anaerobic bacteria (p.gingivalis, t.forsythia, t.denticola, p.intermedia, f.nucleatum) assosciated with chronic periodontitis present at the implant -abutment interface(iai) of healthy implants and implants affected by peri-implantitis for at least one year.

1st author and year	Bacteria	Standard deviation	Mean	Variance	Upper limit	Lower limit	P-value	Z-value
Peri-implantitis								
1. Canullo et al.[5]	P. gingivalis	0.186	3.377	0.035	3.747	3.012	0.000	18.154
2. Canullo et al.[7]	T. forsythia	0.158	2.388	0.025	2.697	2.079	0.000	15.124
	T. denticola	0.185	2.641	0.034	3.003	2.279	0.000	14.281
	P. intermedia	0.192	4.410	0.037	4.786	4.034	0.000	22.966
	F. nucleatum	0.120	5.600	0.014	5.836	5.364	0.000	46.507
Total		0.088	3.516	0.008	3.689	3.344	0.000	40.409
Healthy implants								
1. Canullo et al.[5]	p. gingivalis	0.157	2.475	0.024	2.782	2.169	0.000	15.815

2. Canullo et al.[7]	T. forsythia	0.135	2.783	0.018	2.047	2.519	0.000	20.648
3. Penarrocha oltra et al.[33]	T .denticola	0.148	1.685	0.022	1.975	1.395	0.000	11.398
4. Jervøe-storm et al.[27]	P. intermedia	0.167	3.543	0.028	3.870	3.217	0.000	21.279
5. Canullo et al.[34]	F. nucleatum	0.106	5.193	0.011	5.401	4.986	0.000	48.977
Total		0.075	2.971	0.006	3.118	2.824	0.000	39.555

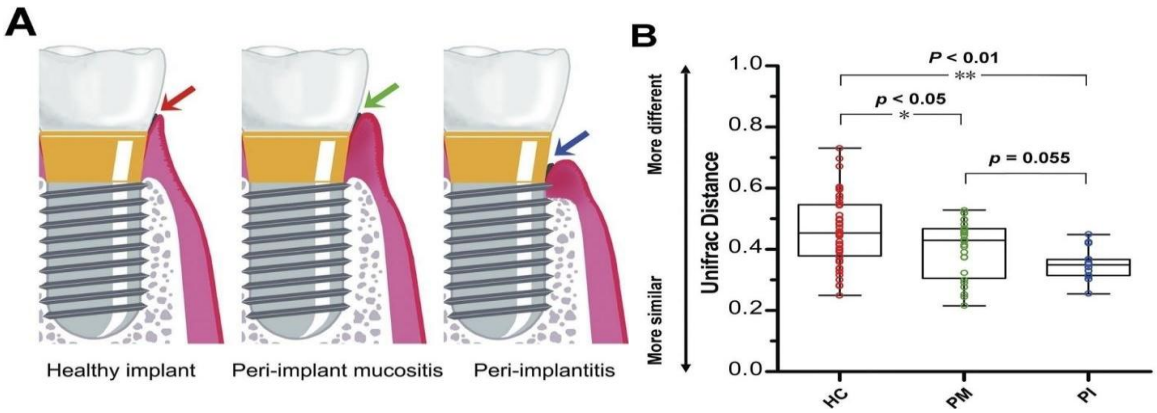


Fig. 3: Healthy peri-implant conditions vs peri-implantitis.

Table 3: Meta-analysis.

	STD ERROR	STD DIFFERENCE IN MEANS	VARIANCE	UPPER LIMIT	LOWER LIMIT	P-VALUE	Z-VALUE
Pg	0.124	0.484	0.015	0.728	0.241	0.000	3.984
Td	0.124	0.484	0.015	0.728	0.241	0.000	3.984
Fn	0.123	0.307	0.015	0.548	0.065	0.013	2.486
Tf	0.123	0.183	0.015	0.424	-0.058	0.137	1.488
Pi	0.124	0.484	0.015	0.728	0.241	0.0	3.984

4. DISCUSSION

Most of the dental implants have a pair of components: the implant placed inside the bone and collectively the abutment screwed into the implant throughout the surgical technique to support rehabilitation. This systemic review estimates its substantial risk of peri-implantitis due to its colonization of microorganisms at the IAI on bone level implants. One-piece implants were excluded from studies because of its supracrestal position of their IAJ and due to its aerobic environment causing a significant difference in microbiological composition. However, due to the formation of biofilm in their location biological process of bone is established in the initial stage of the prosthetic load. In the current review, a considerably higher number of bacteria was noticed at implants for all gram-negative periodontal pathogens affected by peri-implantitis in comparision to healthy peri-implant sulcus, apart from T. forsythia. Thus for T. forsythia, drift towards higher bacterial colonization was detected.

The studies evaluated the microbiota who received two-stage bone level implant systems at the level of IAI in patients with several implant-abutment connection designs. The 2 studies.[25,34] apart from the connection design recorded the contamination of the IAI. No difference from screw and cement-retained restorations could be noticed assuming that the crown-abutment junction and the gap filled with cement is located more coronal. Moreover, submerged and non-submerged implants in the colonization of microbes included manuscripts that did not show differences between them.

Demonstration of bacterial contamination at the alveolar bone level of the IAI placed resulted in a substantial increase in bone loss and inflammatory cell infiltration.[27] The persistence of chemotactic stimuli showed incessant recruitment of neutrophilic granulocytes by the accumulation of acute inflammatory cells adjacent to the IAI position.[38,39] Moreover, microbial contamination was also led at the implant-abutment interfaces by the presence of inflammatory infiltration of peri-implant tissue.[24,26]

Various studies noticed that both the healthy and diseased tissue conditions showed microbial

contamination at the level of IAI.[5,7,40] Apart from the fact that no clinical signs of peri-implantitis could be seen, the microbial species related to this condition were noticeable. When implants with healthy or peri-implantitis tissue conditions were estimated and data from healthy and diseased implant sites were compared with the clinical and microbiological features in subjects within the same subject (534 patients; 1507 dental implants), noticeable trends were witnessed.[5] Microbial analysis gathered from 3 locations (peri-implant sulcus (PIS), implant connections of the inner parts (PI), gingival sulcus of the adjacent teeth) in context with clinical parameters (bleeding on probing, pocket depth, plaque index), peri-implantitis was significantly visible in 10.3% of the patients and 7.3% of the implants. 53 patients affected by peri-implantitis during the microbial analysis showed that no significant differences between the analysis at the PIS and PI were noticed.[5]

Microgap including the fractures of the abutment screw and peri-implant diseases may also lead to mechanical and biological complications at the IAI.[25] Micro-leakage and the microgap size at the IAI of 4 various abutments to Straumann implants denoted substantial effect within the first 5h of the experiment ($p=0.012$) with the mean microgap size ($p<0.001$) and the mean number of bacterial colonization (CFU/mL) leaking.[25] However, the micro-leakage at 24h, 48h, and 14days no longer upsurged significantly ($p=0.145$).

Clinical and microbial differences resulted that the microbial predominance was higher in the peri-implantitis group at 3 locations between healthy peri-implant conditions and the differences between various types of bacteria were pointed within the connection than in the PIS (57 patients; 122 implants).[5] Opportunistic pathogens such as E. faecalis, P. aeruginosa at the level of PIS of each implant were noticed in the presence of the peri-implant condition, gingival sulcus of the adjacent teeth and the abutment connection within each implant shows the substantial variances of nosocomial bacteria around the diseased implants.[35] This suggests the prominence of decontamination of the abutment connection with treatment to peri-implantitis.

Various attempts to reduce the colonization of bacteria at the IAI were proposed with healthy implants. However, 0.2% chlorhexidine solution application at 2 stage surgeries is suggested to be more common in practice. Though, controversial opinions still exist on the application of chlorhexidine solution for preventing microbial colonization at the IAI.[45,46] 0.2% chlorhexidine solution could not considerably eliminate the penetration of bacterial endotoxins at the IAJ for a long time. On the contrary, no indications for implants affected by peri-implantitis were also provided in the Literature review.

4 CONCLUSION

Scientific articles on prosthetic risk factors such as peri-implantitis are very rare. This meta-analysis showed that bacteria at the implant-abutment interface could easily be colonized. It is significantly evident that inner portions of IAI should always be considered contaminated from a clinical point of view, even in clinically healthy patients.

5 ACKNOWLEDGMENT

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