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Targeted Antimicrobial Therapy for Rapid Osseointegration Loss in Peri-implantitis: A Prospective Study of the Qualitative Bacterial Etiology, Clinical Management and Treatment Protocols.

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Peri-implantitis; bacterial infection; osseointegration loss; Prospective study; antibiotic resistance; Targeted Antimicrobial Therapy.

Abstract

Background: Dental implants are affected by peri-implantitis, an inflammatory condition that can lead to rapid bone loss and implant failure. This prospective study investigated the qualitative bacterial etiology of peri-implantitis, a particularly aggressive form of the disease.

Methods: This prospective study included 26 patients (aged 23-45) with healthy, functional implants in service for at least 12 months, who presented with acute infection. Patients were divided into two groups based on reverse torque testing values. Group I (n=12) consisted of implants with a reverse torque value of less than 15 Ncm, indicating reduced rotational stability and more severe implantitis. Group II (n=12) consisted of implants with a reverse torque value of 15 Ncm or greater, indicating adequate rotational stability and less severe implantitis. Group I implants were explanted for bacterial culture. Group II implants underwent supra-structure removal, debridement, laser disinfection, and bacterial swabbing. All patients were examined for primary infection sources (periodontal, endodontic, or other), which were managed accordingly. Bacterial specimens were cultured and identified.

Results: Seven bacterial strains were identified: *Porphyromonas gingivalis, methicillin-resistant Staphylococcus aureus (MRSA), Aggregatibacter actinomycetemcomitans, Enterococcus faecalis, Prevotella intermedia, Pseudomonas aeruginosa, and Serratia marcescens*. Many specimens exhibited antibiotic resistance, requiring tailored combination therapies. Grade I patients received new implants after 8 weeks; Grade II patients received new abutments/restorations after 6 weeks. Bacterial species from primary infection sources matched those from affected implant sites.

Conclusion: Peri-implantitis is associated with aggressive, often antibiotic-resistant bacterial infections, including MRSA. Early diagnosis, pathogen identification, and targeted antimicrobial therapy, along with management of primary infection sources, are essential for preventing rapid osseointegration loss and implant failure. Further studies are needed to quantify the bacterial burden in these infections.

1 Introduction

Dental implants have become a reliable and popular treatment option for replacing missing teeth. While generally successful, with reported 10-year success rates of 90-95% [1], complications can occur and pose significant challenges. Among these, peri-implantitis, an inflammatory condition affecting the tissues surrounding the implant, is a major concern. Peri-implantitis can lead to bone loss, implant instability, and ultimately, implant failure. The reported prevalence of peri-implantitis varies widely,

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ranging from 1% to 47% in a meta-analysis by Derks et al. [2], with a more recent study by Vignoletti et al. [3] reporting a prevalence of 35%.

Peri-implantitis is characterized by inflammation, bleeding on probing and/or suppuration, detectable bone loss exceeding 2mm beyond initial remodeling, and probing depths of 4mm or greater [4]. Peri-implant diseases encompass a spectrum of inflammatory processes affecting both the soft and hard tissues surrounding implants. Several classification systems have been developed to categorize peri-implant lesions. These classifications consider factors such as the activity of the lesion (active vs. inactive) [5], the extent of bone loss [6], the location of the lesion (apical vs. marginal) [7], and the source of infection (tooth-to-implant vs. implant-to-tooth). [8]

A critical factor in peri-implantitis development is the concept of endo-implant cross-infection, initially described by Daubert *et al*..[9] This refers to infection spreading from an adjacent tooth with an endodontic infection to the nearby implant. Clinically, this cross-infection can mimic peri-implantitis, presenting with mucositis and marginal bone loss. However, radiographic examination can often reveal the infectious pathway connecting the tooth and implant, differentiating it from true peri-implantitis. This cross-infection is essentially a biofilm-mediated process [10], where a complex community of bacteria encased within an extracellular matrix adheres to the implant or tooth surface. Biofilm formation is a multi-stage process involving attachment, growth, maturation, and dispersal.[11] Periapical pathosis in adjacent teeth has been implicated in up to 25% of implant failures [12], and the incidence of retrograde peri-implantitis (periapical bone loss around the implant within the first 6 months) is increased in the presence of adjacent tooth periapical infection. [13]

Treatment strategies for peri-implantitis encompass non-surgical approaches (mechanical debridement, antiseptics, and antibiotics), surface decontamination (air abrasives, chemical agents, laser irradiation) [14,15], and surgical interventions (resective and regenerative techniques).[16] While mechanical debridement is essential, it is often insufficient to eliminate the causative bacteria completely. Therefore, combination therapies involving antiseptics and/or surgical interventions are often necessary. Surface decontamination methods like laser treatment or air abrasion can be helpful, but their long-term effectiveness requires further investigation. Surgical interventions, including pocket reduction, bone recontouring, and meticulous plaque control, have demonstrated efficacy in managing peri-implantitis. [16] Critically, addressing the primary source of infection is paramount to successful treatment. [17]

Several bacterial species have been implicated in peri-implantitis, including *Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus faecalis, and Pseudomonas aeruginosa.* [18] These bacteria are commonly found in oral biofilms and can cause both acute and chronic infections, not only in dental implants but also in orthopedic implants. The connection between dental infections and other distant site infections is also recognized. For example, dental infections have been identified as a source of hematogenous spread to prosthetic joint replacements, contributing to approximately 15% of peri-prosthetic joint infections. [19]

A particularly challenging form of peri-implantitis is the rapidly destructive variant. In these cases, a previously healthy and functional implant can rapidly become mobile due to acute destruction of the surrounding bone. The rapid progression of this infection often necessitates implant removal if diagnosis and treatment are delayed.[17] This study aimed to highlight a strong correlation between qualitative bacterial species found at primary infection sites and their etiology to affected implant sites. This underscores the importance of targeted antimicrobial therapy and primary infection management in preventing rapid osseointegration loss and implant failure in peri-implantitis.

2 Materials and Methods

2.1 Ethical Approval

The method employed in this study was approved by the research ethical committee (Faculty of Dentistry - MSA University). The research was granted confirmation of conductance number (52114), and all participants provided written informed consent, with the right to withdraw from the study at any time. The study was conducted at the Restorative and Oral Pathology Department, Faculty of Dentistry, MSA University, between (June,2022) and (August,2024). Ethical considerations were paramount, with adherence to the Declaration of Helsinki.

2.2 Study design

This prospective study investigated the bacterial strains associated with peri-implant infections and evaluated different treatment protocols for these infections **Table 1**.

Table 1. Summary Statistics of Demographics by Group with P-Value

Group	Gender	Count by gender	Age (mean ± SD)
Grade 1 Infection Group	F	6	31.69 ± 7.35
	M	7	
Grade 2 Infection Group	F	6	34 ± 7.42
	M	7	
p-value	1		0.43
Note: SD (standard deviation)			

Twenty-Six patients meeting specific inclusion criteria were recruited from those presenting with functioning delayed implants, which were loaded with the prosthetic part after 3 months, that had been in service for at least 12 months. The study included individuals aged 23 to 45 years who had recently developed pain or mobility associated with their implant or superstructure and maintained good oral hygiene. Exclusion criteria encompassed smoking, presence of immunocompromising diseases, and significant bone loss.

2.3 Eligibility Criteria:

Inclusion Criteria:

Presence of a functioning delayed implant (loaded after 3 months) that had been in service for at least 12 months, Recent onset of pain or mobility related to the implant or superstructure, Age between 23 and 45 years, and Good oral hygiene.

Exclusion Criteria:

Smoking, Immuno-compromising diseases, severe bone loss, Uncontrolled diabetic patients, Heavy Smokers above 10 cigarettes per day.

Patients exhibiting severe bone loss were excluded to minimize the influence of pre-existing bone deficiencies on the study's outcomes. Severe bone loss can negatively impact implant osseointegration and long-term stability, potentially leading to increased failure rates. [21]

2.4 Allocation of Participants

Patients underwent initial clinical and radiographic examinations to confirm the presence of implant-related issues. Implant mobility, specifically quantified using reverse torque testing, served as the primary grouping criterion. Patients were assigned to one of two groups based solely on the results of the reverse torque testing.

Group 1: Grade I Infection: This group comprised patients exhibiting implants with more than 2mm of mobility in any direction, pain on pressure, and radiographic evidence of early bone loss surrounding the affected implant 12 months immediately following implant placement, during which bone loss was assessed. These patients underwent aseptic implant removal, bacterial culture of the explanted implant, thorough curettage and cleaning of the extraction socket, and suturing. Post-operatively, they received chlorhexidine mouthwash and analgesics.

Group 2: Grade II Infection: This group included patients whose implants demonstrated at least 15 Ncm of torque resistance. Radiographic examination revealed some signs of inflammation but without severe bone loss. These patients also reported pain on pressure and soreness in the jawbone surrounding the affected implant. Their treatment consisted of supra-structure (abutment and restoration) removal, bacterial swabbing from the implant neck area, cover screw placement, a small crestal incision, soft tissue curettage, and cleaning, irrigation, and diode laser disinfection of the implant periphery. Following bacterial culture results, patients received tailored combination antibiotic therapy. **Table 2**.

Table 2. Grouping Criteria

Group	Description	Treatment
Grade I Infection Group	Severe Peri-implantitis: Likely characterized by significant bone loss, implant mobility, and/or pain.	This required explantation. Implant removal, curettage of extraction socket, suturing, chlorhexidine mouthwash, analgesics. New implant placement after 8 weeks.
Grade II Infection Group	Less Severe Peri-implantitis: Likely characterized by some inflammation and perhaps minor bone loss, but the implant was stable enough to be salvaged.	Supra-structure removal, bacterial swabbing, cover screw placement, crestal incision, curettage, cleaning/irrigation, laser disinfection. New abutment and restoration after 6 weeks (after infection resolution).

2.5 Management of Primary Infection Source

To ensure comprehensive patient care and eliminate potential sources of cross-infection that could compromise long-term implant health, all patients underwent a thorough oral examination. This included assessment for periodontal disease, caries, pulpitis, and periapical infections. The presence of these conditions did not exclude patients from the study; instead, they were addressed according to a detailed, pre-established protocol. Acute and chronic periodontal infections were treated with deep pocket debridement, consisting of scaling and root planing using ultrasonic tips with povidone-iodine irrigation, gingival curettage with Gracey curettes to remove necrotic and granulation tissue, saline irrigation, and application of metronidazole gel to the infected pockets.

All periodontal procedures were performed by a single, calibrated operator to

standardize treatment. Non-restorable teeth, defined as those presenting with extensive caries, significant bone loss, furcation involvement, or other factors precluding successful restorative or endodontic intervention, were extracted. While patients demonstrated good oral hygiene at screening, these non-restorable teeth, along with other identified dental infections, could contribute to the overall microbial burden and negatively impact implant outcomes. Therefore, their extraction was deemed necessary. Carious lesions were restored, and defective existing restorations were replaced. Vital teeth with pulp exposure received endodontic treatment, including local anesthesia (4% articaine with 1:100,000 epinephrine), access cavity preparation, canal instrumentation using a crown-down technique with ProTaper Gold files, and obturation with bio-sealer coated gutta-percha cones. Periapical infections were managed with root canal retreatment, involving gutta-percha removal with Gates Glidden burs and solvent, copious NaOCl irrigation, and a 10-day calcium hydroxide dressing (UltraCal XS).

2.6 Bacterial Culture Procedures

Bacterial samples were collected from three sources: extracted implants (Grade I), the implant-bone interface (Grade II), and infected root canals (including those from extracted teeth). For Grade I implants, explanted specimens were rinsed with saline to remove debris and planktonic bacteria before being placed in sterile tubes for processing and identification [22]. Samples from the implant-bone interface of Grade II implants were collected using sterile swabs and a no-touch technique to minimize contamination, then transported in sterile containers for processing within two hours [23]. Root canal samples were collected after rubber dam isolation and access cavity preparation (without water spray). Canals were enlarged with K-files, and sterile paper points were inserted for 60 seconds to absorb samples, which were then transferred to transport medium [24]. This same paper point method was used for sampling infected root canals from extracted teeth. Following bacterial identification, antibiotic susceptibility testing was performed. Disc diffusion assays provided an initial assessment of resistance to common antibiotics. Isolates showing resistance or intermediate susceptibility then underwent broth microdilution assays to determine minimum inhibitory concentrations (MICs) for a wider range of antibiotics. Clinical guidelines and known resistance patterns informed antibiotic selection for testing, and MIC results guided patient-specific combination antibiotic therapies.

2.7 Targeted Antibiotic Therapy

Following bacterial identification and antibiotic sensitivity testing, each patient received a tailored combination antibiotic therapy, which successfully controlled the infections in all cases. Specifically, patients infected with methicillin-resistant Staphylococcus aureus (MRSA) were prescribed vancomycin 125 mg four times a day for 10 days. For infections involving Pseudomonas aeruginosa and/or Enterococcus faecalis, the regimen consisted of amoxicillin and clavulanate 1.0 g, followed by a maintenance dose of 500 mg three times a day for three days. Patients with Serratia marcescens infections received a single dose of aminoglycosides for two days, combined with a fourth-generation cephalosporin.

3 Results

Ten patients presented with Grade I peri-implantitis, requiring implant removal and replacement, while thirteen patients with Grade II peri-implantitis received new restorations after six weeks. The primary infection source was identified as a necrotic or failed endodontically treated tooth in fifteen cases, periodontal infection in five, and a non-dental source in three. **Table 3.**

Table 3. Cell culture results of infected implants and the proposed line of treatment

Bacterial type	Location of implant	Type of infection	Source of infection	Characteristics	Virulence	Antibiotics
Porphyromonas gingivalis	46, 36, 25, 14, 17	Grade I	Endodontically treated tooth	Non-motile, Gram-negative, rod-shaped, anaerobic, pathogenic bacterium. Forms black colonies on blood agar.	Collagenase production cause rapid damage to infected tissues	Amoxicillin + clavulanate 1.0 g followed by a maintenance dose of 500 mg t.i.d. for 3 days,
Methicillin-resistant Staphylococcus aureus	36, 47,46,		Systemic infection	Gram-positive, spherical shaped microorganism, non-motile, non-spore former, and some strains are capsulated.	Capsular polysaccharides impaire complement and antibody-mediated opsonization and inhibiting phagocytosis	Vancomycin 125 milligrams (mg) 4 times a day for 10 days.
Aggregatibacter actinomycetemcomitans	24, 25, 27	Grade I	Periodontal infection	Gram-negative, facultative anaerobe, nonmotile bacterium	Pore-forming toxin leukotoxin A attaching white blood cells expressing integrin beta-2 (CD18)	Moxifloxacin 400 milligrams (mg) once every 24 hours 5-10 days
Pseudomonas aeruginos	16, 17, 35	Grade II	Necrotic tooth	Encapsulated, Gram-negative, aerobic-facultatively anaerobic, rod-shaped bacterium	Lipopolysaccharide tissue damage by endotoxicity	Amoxicillin + clavulanate 1.0 g followed by a maintenance dose of 500 mg t.i.d. for 3 days,
Prevotella intermedia	35, 37,11	Grade I	Failed endodontic treatment	Black-pigmenting anaerobe	Require haemin as source of iron, and binds to lactoferrin	Amoxicillin + clavulanate 1.0 g followed by a maintenance dose of 500 mg t.i.d. for 3 days, and Metronidazole 250 mg TID for 7 days.
Enterococcus faecalis	16, 15, 35	Grade II	Failed endodontic treatment	Non-motile, gram-positive, commensal bacterium inhabiting the gastrointestinal tracts	Releases lytic enzymes, cytolysin, aggregation substance, pheromones, and lipoteichoic acid	Ampicillin, vancomycin, gentamicin, ceftriaxone
Serratia marcescens	36, 46, 35		Periodontal infection	Rod shaped gram negative bacterial associated with hospital and wound infections	DNase, lipase, gelatinase, hemolysin, proteases, chitinase, chloroperoxidase, and multiple isozymes of alkaline phosphatase	Aminoglycosides in combination fourth-generation cephalosporins

Bacterial cultures consistently revealed aggressive, highly antibiotic-resistant strains. Notably, bacterial species cultured from explanted implants (Grade I) and the implant-bone interface (Grade II) matched those found in concurrently sampled infected root canals, when present. Seven bacterial species were identified: Porphyromonas gingivalis, methicillin-resistant Staphylococcus aureus (MRSA), Aggregatibacter actinomycetemcomitans, Enterococcus faecalis, Prevotella intermedia, Pseudomonas aeruginosa, and Serratia marcescens. Following antibiotic sensitivity testing, tailored combination antibiotic therapies were administered, successfully controlling all infections.

Figure 1A. Grade I implant infection due to post extraction infection of mandibular right molar.

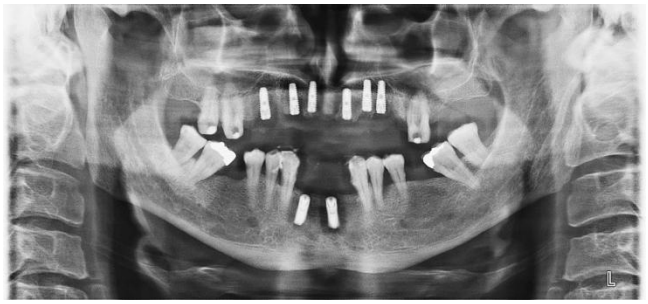

Figure 1B. Grade I implant infection due to periodontal abscess infecting implant in position mandibular left Incisor area.

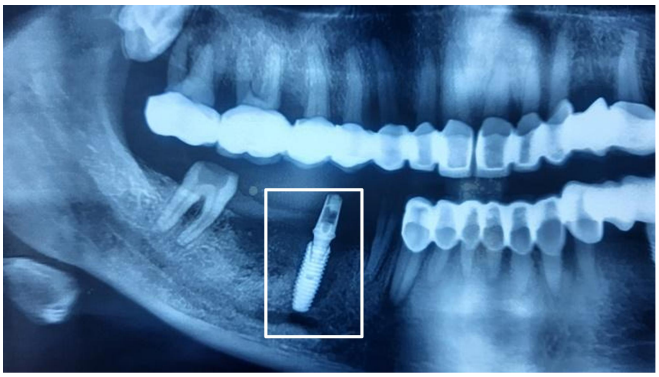

Figure 1C. Grade I implant infection due to bacterial load related to exposed lower right molar.

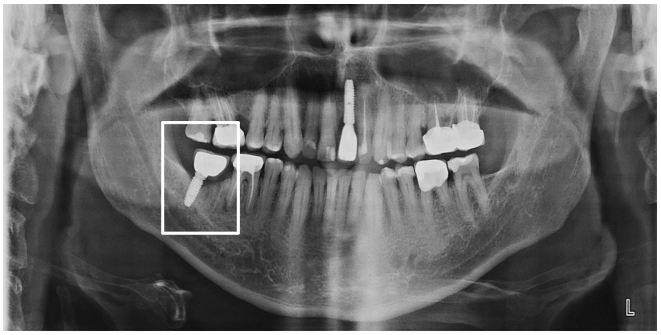

Figure 2A. Grade II implant infection due failed root canal treatment of lower right molar.

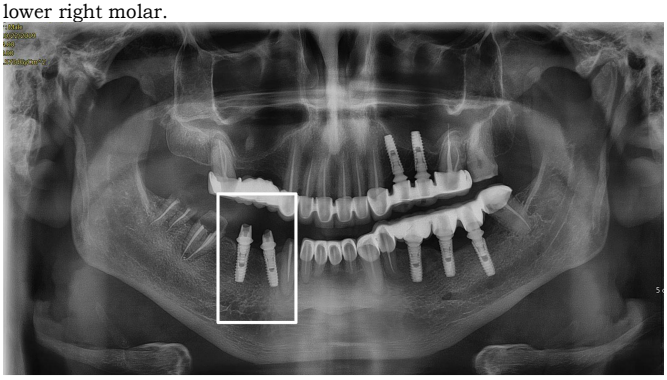

Figure 2B. Grade II implant infection due failed root canal treatment of lower right second molar.

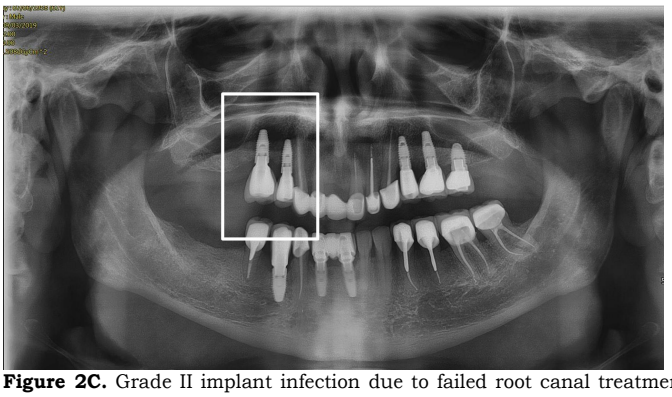

Figure 2C. Grade II implant infection due to failed root canal treatment of upper right canine.

4 Discussion

This study identified seven bacterial strains associated with peri-implantitis: *Porphyromonas gingivalis, methicillin-resistant Staphylococcus aureus(MRSA), Aggregatibacter actinomycetemcomitans, Enterococcus faecalis, Prevotella intermedia, Pseudomonas aeruginosa, and Serratia marcescens*. The rapid implant loss observed in ten cases underscores the aggressive nature of these infections and the importance of prompt diagnosis and treatment. These findings align with existing literature describing retrograde peri-implantitis, particularly its association with endodontic infections in adjacent teeth. [25,26] While the prevalence of retrograde peri-implantitis is reported to be relatively low (0.26%–1.86%), it increases significantly in the presence of an adjacent endodontically treated tooth (up to 7.8%) [25,26], highlighting the clinical relevance of this cross-infection pathway.

The role of bacterial biofilms in peri-implant infections, including retrograde peri-implantitis, is well-

established. Biofilm formation is a complex, multi-stage process [27] involving bacterial adhesion, growth, maturation, and dispersal. Numerous bacterial species can be found in and around the apices of endodontically treated teeth.[28] During endodontic treatment failure, the microbial flora often shifts to a polymicrobial community dominated by gram-positive facultative anaerobes, notably *Enterococcus faecalis*. [29,30]

E. faecalis possesses several mechanisms that contribute to its persistence in challenging environments, including its ability to adhere to dentin [31], survive in trabecular bone [32], and resist both antibodies and antimicrobials within its self-encapsulated biofilm.[32] This resilience allows *E. faecalis* to survive in energy-starved root canals [33] and even in bone after tooth extraction, potentially colonizing implants placed in extraction sites or adjacent to existing periapical infections. [34] The initial interaction between bacteria and the implant surface is influenced by physiochemical properties like hydrophobicity and electrostatic charge.[35] High hydrophilicity promotes bacterial adhesion and aggregation, leading to biofilm formation and encapsulation within a protective matrix that enhances bacterial survival. Biofilm maturation is dependent on nutritional factors, such as glucose availability, and cells may detach from the biofilm surface when nutrients become scarce.[27]

In this study, *P. gingivalis* was frequently identified, suggesting a strong association with symptomatic infected pulps or peri-radicular diseases in adjacent teeth.[36] *P. gingivalis* is a common component of complex multispecies biofilms in both root canal and periodontal infections. Its virulence factors, including caseinolytic proteases (Clp) enzymes, contribute to tissue damage and biofilm formation.[37] The high prevalence of *P. gingivalis* in this study reinforces the importance of managing existing dental infections before implant placement to prevent cross-infection. While a combined antibiotic regimen of amoxicillin, clavulanate, cefoxitin, and imipenem has been suggested for *P. gingivalis* infections [38], antibiotic sensitivity testing is crucial to ensure appropriate treatment.

The notable presence of MRSA in this study is a significant concern. The emergence of drug-resistant *S. aureus* strains, including MRSA, poses a serious challenge in oral infections.[39] *S. aureus* biofilms, composed of water, bacterial microcolonies, and an extracellular polymeric substance containing polysaccharides, extracellular DNA, and proteins like clumping factors A and B [40], contribute to their persistence and resistance to antimicrobials. *S. aureus's* affinity for implant surfaces, mediated by microbial surface components recognizing adhesive matrix molecules (MSCRAMMs) [13], further complicates peri-implant infections. This affinity, coupled with increased implant surface roughness promoting biofilm formation, emphasizes the need for meticulous management of periapical infections in adjacent teeth, particularly before implant placement in cases with a lower implant prognosis. While vancomycin remains a common treatment option for MRSA infections [41], antibiotic susceptibility testing is essential to guide therapy.

The presence of *A. actinomycetemcomitans* is consistent with its known role in localized aggressive periodontitis (LAP). [42,43] *P. aeruginosa*, known for its ability to form biofilms on both biotic and abiotic surfaces, is a frequent isolate in refractory root canal infections [44] due to its facultative anaerobic nature and denitrifying capacity [45-47]. *Prevotella intermedia*, another common isolate, can be treated with metronidazole, azithromycin, or beta-lactam antibiotics plus beta-lactamase inhibitors. [48] *E. faecalis'* involvement in post-treatment apical periodontitis [49] and its ability to develop antibiotic resistance through horizontal gene transfer within biofilms highlight the challenges in eradicating this organism. *S. marcescens*, while less common in the oral cavity, has been isolated from subgingival biofilms [50] and exhibits resistance to several antibiotics [50], underscoring the importance of tailored antibiotic therapy. The microbial composition of peri-implantitis can differ from that of periodontitis. [51] While both often involve gram-negative bacteria, peri-implantitis can also harbor opportunistic microorganisms like *S. aureus, Streptococcus anaerobius, E. coli, Candida,* and various *Streptococci spp.* The low infection rates associated with orthopedic implants [52] contrast with the challenges seen in peri-implantitis, likely due to differences in the surrounding tissues and the potential for oral flora to contribute to infection. Hematogenous spread from distant infection sites, including dental infections, to orthopedic implants is a recognized phenomenon [19], emphasizing the interconnectedness of systemic and oral health.

The mechanisms of bone destruction in peri-implantitis involve osteoclastogenesis, a process regulated by RANKL and influenced by bacterial LPS via TLR4 on osteoblasts [53]. Acute inflammatory pathways likely contribute to rapid bone loss in Grade I infections. Osteoclasts, expressing TRAP and utilizing $\alpha V\beta 3$ integrin receptors, attach to bone surfaces and release proteolytic enzymes like cathepsin K, facilitating bone resorption [54]. These cellular and molecular mechanisms explain the rapid destruction observed in peri-implantitis. The reverse torque test is a valuable tool in implant dentistry, providing a quantifiable measure of primary stability. Unlike subjective assessments, it objectively measures the torque needed to initiate reverse rotation, enabling precise evaluation of initial implant anchorage. This is crucial for early detection of

instability, a major risk factor for early failure, allowing timely intervention. The test reflects the mechanical bond between implant and bone, especially important in compromised bone quality. While primarily used at placement, it can sometimes monitor healing. [55]

5 Conclusion

Within the limitations of this study:

In this prospective study, seven bacterial strains (P. gingivalis, MRSA, A. actinomycetemcomitans, E. faecalis, P. intermedia, P. aeruginosa, S. marcescens) were associated with peri-implantitis, highlighting the need for prompt intervention and tailored antibiotic therapy.

Rapid implant failure underscore the importance of considering endodontic cross-infection, tailoring antibiotic therapy based on sensitivity testing due to prevalent antibiotic resistance, and a comprehensive treatment approach encompassing source control, debridement, and targeted antimicrobials.

Future studies should evaluate treatments and quantify bacterial load, which was a limitation of this initial investigation.

Authors' Contributions

Hinar Hani Al Moghazy made a substantial contribution to the study idea, clinical work, data collection, data analysis, data interpretation, manuscript drafting

Hadiel Mohamed Zamzam helped in data collection, data interpretation, manuscript revision.

Moataz-Bellah Ahmed Alkhawas helped in data analysis, manuscript drafting.

Moustafa Nabil Aboushelib contributed in the study idea, data analysis, data interpretation, manuscript revision.

All authors have read and approved the manuscript.

Conflict of interest

The authors declare that they hold no competing interests.

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References

[1] Tricio J, Laohapand P, van Steenberghe D, Quirynen M, Naert I. Mechanical state assessment of the implant-bone continuum: a better understanding of the Periotest method. Int J Oral Maxillofac Implants. 1995 Jan-Feb;10(1):43-9. PMID: 7615316.

[2] Derks, J.; Tomasi, C. Peri-implant health and disease. A systematic review of current epidemiology. J. Clin. Periodontol. 2015, 42 (Suppl. S16), S158–S171.

[3] Vignoletti, F.; Di Domenico, G.L.; Di Martino, M.; Montero, E.; de Sanctis, M. Prevalence and risk indicators of peri-implantitis in a sample of university-based dental patients in Italy: A cross-sectional study. J. Clin. Periodontol. 2019, 46, 597–605.

[4] Daubert DM, Weinstein BF, Bordin S, Leroux BG, Flemming TF. Prevalence and predictive factors for peri-implant disease and implant failure: a cross-sectional analysis. J Periodontol 2015; 86: 337–347.

[5] Reiser GM, Nevins M. The implant periapical lesion: etiology, prevention, and treatment. Compend Contin Educ Dent. 1995 Aug;16(8):768, 770, 772 passim. PMID: 8620395.

[6] Shah R, Thomas R, Kumar AB, Mehta DS. A Radiographic Classification for Retrograde Peri-implantitis. The journal of contemporary dental practice. 2016; 17(4):313–21.

[7] Kadkhodazadeh M, Amid R. A New Classification for the Relationship between Periodontal, Periapical, and Peri-implant Complications. Iranian endodontic journal. 2013; 8(3):103–8.

[8] Sussman HI. Periapical implant pathology. The Journal of oral implantology. 1998; 24(3):133–8.

[9] Gong J, Al-Sosowa AA, Zhao R, Li J, Mei M. Successful Management of Peri-Implant Infection from the Endodontic Lesion of Adjacent Natural Tooth. Case Rep Dent. 2023 Mar 14;2023:5034582. doi: 10.1155/2023/5034582. PMID: 36960122; PMCID: PMC10030217.

[10] Neelakantan P, Romero M, Vera J, Daood U, Khan AU, Yan A, Cheung GSP. Biofilms in Endodontics-Current Status and Future Directions. Int J Mol Sci. 2017 Aug 11;18(8):1748. doi: 10.3390/ijms18081748. PMID: 28800075; PMCID: PMC5578138.

[11] Silva V, Almeida L, Gaio V, Cerca N, Manageiro V, Caniça M, Capelo JL, Igrejas G, Poeta P. Biofilm Formation of Multidrug-Resistant MRSA Strains Isolated from Different Types of Human Infections. Pathogens. 2021 Jul 30;10(8):970. doi: 10.3390/pathogens10080970. PMID: 34451434; PMCID: PMC8400568.

[12] Lefever D, Van Assche N, Temmerman A, Teughels W, Quirynen M. Aetiology, microbiology and therapy of periapical lesions around oral implants: a retrospective analysis. J Clin Periodontol. 2013 Mar;40(3):296-302. doi: 10.1111/jcpe.12045. Epub 2012 Dec 27. PMID: 23278599.

[13] Di Murro B, Papi P, Di Murro C, Pompa G, Gambarini G. Correlation between endodontic pulpal/periapical disease and retrograde peri-implantitis: A case series. Aust Endod J. 2021 Aug;47(2):358-364. doi: 10.1111/aej.12458. Epub 2020 Nov 7. PMID: 33159493.

[14] Schwarz F, Schmucker A, Becker J. Efficacy of alternative or adjunctive measures to conventional treatment of peri-implant mucositis and peri-implantitis: a systematic review and meta-analysis. Int J Implant Dent. 2015 Dec;1(1):22. doi: 10.1186/s40729-015-0023-1. Epub 2015 Aug 13. PMID: 27747644; PMCID: PMC5005629.

[15] Khoury F, Keeve PL, Ramanauskaite A, Schwarz F, Koo KT, Sculean A, Romanos G. Surgical treatment of peri-implantitis–Consensus report of working group 4. International dental journal. 2019 Sep;69:18-22. doi: 10.1111/idj.12505.

[16] Rokaya D, Srimaneepong V, Wisitrasameewon W, Humagain M, Thunyakitpisal P. Peri-implantitis Update: Risk Indicators, Diagnosis, and Treatment. Eur J Dent. 2020 Oct;14(4):672-682. doi: 10.1055/s-0040-1715779. Epub 2020 Sep 3. PMID: 32882741; PMCID: PMC7536094.

[17] Gong J, Al-Sosowa AA, Zhao R, Li J, Mei M. Successful Management of Peri-Implant Infection from the Endodontic Lesion of Adjacent Natural Tooth. Case Rep Dent. 2023 Mar 14;2023:5034582. doi: 10.1155/2023/5034582. PMID: 36960122; PMCID: PMC10030217.

[18] Arciola CR, Campoccia D, Montanaro L. Implant infections: adhesion, biofilm formation and immune evasion. Nat Rev Microbiol. 2018 Jul;16(7):397-409. doi: 10.1038/s41579-018-0019-y. PMID: 29720707.

[19] Rakow A, Perka C, Trampuz A, Renz N. Origin and characteristics of haematogenous periprosthetic joint infection. Clin Microbiol Infect. 2019 Jul;25(7):845-850. doi: 10.1016/j.cmi.2018.10.010. Epub 2018 Oct 26. PMID: 30678837.

[20] Aimetti M. Nonsurgical periodontal treatment. Int J Esthet Dent. 2014 Summer;9(2):251-67. PMID: 24765632.

[21] Bressan E, Zucchelli G, Tommasato G, Pesce P, Canullo L, Consensus Meeting Group Iao, Grusovin MG. Consensus Report by the Italian Academy of Osseointegration on the Importance of Peri-Implant Soft Tissues. Medicina (Kaunas). 2024 Aug 26;60(9):1393. doi: 10.3390/medicina60091393. PMID: 39336434; PMCID: PMC11433715.)

[22] Jiang N, Hu YJ, Lin QR, Chen P, Wan HY, He SY, Stoodley P, Yu B. Implant surface culture may be a useful adjunct to standard tissue sampling culture for identification of pathogens accounting for fracture-device-related infection: a within-person randomized agreement study of 42 patients. Acta Orthop. 2022 Sep 7;93:703-708. doi: 10.2340/17453674.2022.4530. PMID: 36069480; PMCID: PMC9450250.

[23] Marshall G, Canullo L, Logan RM, Rossi-Fedele G. Histopathological and microbiological findings associated with retrograde peri-implantitis of extra-radicular endodontic origin: a systematic and critical review. Int J Oral Maxillofac Surg. 2019 Nov;48(11):1475-1484. doi: 10.1016/j.ijom.2019.04.012. Epub 2019 May 11. PMID: 31088705.

[24] Pourhajibagher M, Ghorbanzadeh R, Bahador A. Culture-dependent approaches to explore the prevalence of root canal pathogens from endodontic infections. Braz Oral Res. 2017 Dec 18;31:e108. doi: 10.1590/1807-3107bor-2017.vol31.0108. PMID: 29267669.

[25] Quirynen M, Vogels R, Alsaadi G, et al. Predisposing conditions for retrograde periimplantitis, and treatment suggestions. Clin Oral Implant Res 2005;16:599–608.

[26] Zhou W, Han C, Li D, et al. Endodontic treatment of teeth induces retrograde peri-implantitis. Clin Oral Implants Res 2009;20:1326–1332.

[27] Ran SJ, Jiang W, Zhu CL, Liang JP. Exploration of the mechanisms of biofilm formation by Enterococcus faecalis in glucose starvation environments. Aust Dent J. 2015 Jun;60(2):143-53. doi: 10.1111/adj.12324. Epub 2015 May 20. PMID: 25990488.

[28] Gomes BP, Pinheiro ET, Gadê-Neto CR, Sousa EL, Ferraz CC, Zaia AA, Teixeira FB, Souza-Filho FJ. Microbiological examination of infected dental root canals. Oral Microbiol Immunol. 2004 Apr;19(2):71-6. doi: 10.1046/j.0902-0055.2003.00116.x. PMID: 14871344.

[29] Ran SJ, E J, Zhu CL, He ZY, Liang JP. Effect of different stress conditions on growth and biofilm formation capability of Enterococcus faecalis [in Chinese]. Zhonghua Kou Qiang Yi Xue Za Zhi. 2013;48:529–534.

[30] Molander A, Reit C, Dahlen G, Kvist T. Microbiological status of rootfilled teeth with apical periodontitis. Int Endod J. 1998;31:1–7.

[31] Liu H, Wei X, Ling J, Wang W, Huang X. Biofilm formation capability of Enterococcus faecalis cells in starvation phase and its susceptibility to sodium hypochlorite. J Endod 2010;36:630– 635.

[32] Lo´pez-Martı´nez F, Go´mez Moreno G, Olivares-Ponce P, et al. Implants failures related to endodontic treatment. An observational retrospective study. Clin Oral Implants Res. 2015;26:992–995.

[33] George S, Kishen A, Song KP. The role of environmental changes on monospecies biofilm formation on root canal wall by Enterococcus faecalis. J Endod 2005;31:867–872.

[34] Andrianopoulos A. Control of morphogenesis in the human fungal pathogen Penicillium marneffei. Int J Med Microbiol. 2002;292:331–347.

[35] Bos R, van der Mei HC, Busscher HJ. Physico-chemistry of initial microbial adhesive interactions–its mechanisms and methods for study. FEMS Microbiol Rev 1999;23:179–230.

[36] Tiwari S, Saxena S, Kumari A, Chatterjee S, Hazra A, Choudhary AR. Detection of Red complex bacteria, P. gingivalis, T. denticola and T. forsythia in infected root canals and their association with clinical signs and symptoms. J Family Med Prim Care. 2020 Apr 30;9(4):1915-1920. doi: 10.4103/jfmpc.jfmpc_1177_19. PMID: 32670940; PMCID: PMC7346963.

[37] He L, Wang H, Zhang R, Li H. The regulation of Porphyromonas gingivalis biofilm formation by ClpP. Biochem Biophys Res Commun. 2019 Feb 5;509(2):335-340. doi: 10.1016/j.bbrc.2018.12.071. Epub 2018 Dec 19. PMID: 30579592.

[38] Conrads G, Klomp T, Deng D, Wenzler JS, Braun A, Abdelbary MMH. The Antimicrobial Susceptibility of Porphyromonas gingivalis: Genetic Repertoire, Global Phenotype, and Review of the Literature. Antibiotics (Basel). 2021 Nov 24;10(12):1438. doi: 10.3390/antibiotics10121438. PMID: 34943650; PMCID: PMC8698109.

[39] Al-Akwa, Ameen Abdullah, et al. "Prevalence of staphylococcus aureus in dental infections and the occurrence of MRSA in isolates." Universal Journal of Pharmaceutical Research, May 2020, 23–27.

[40] Idrees M, Sawant S, Karodia N, Rahman A. Staphylococcus aureus Biofilm: Morphology, Genetics, Pathogenesis and Treatment Strategies. Int J Environ Res Public Health. 2021 Jul 16;18(14):7602. doi: 10.3390/ijerph18147602. PMID: 34300053; PMCID: PMC8304105.

[41] Tuon FF, Suss PH, Telles JP, Dantas LR, Borges NH, Ribeiro VST. Antimicrobial Treatment of Staphylococcus aureus Biofilms. Antibiotics (Basel). 2023 Jan 4;12(1):87. doi: 10.3390/antibiotics12010087. PMID: 36671287; PMCID: PMC9854895.

[42] Siqueira JF Jr, Rôças IN. Microbiology and treatment of acute apical abscesses. Clin Microbiol Rev. 2013 Apr;26(2):255-73. doi: 10.1128/CMR.00082-12. PMID: 23554416; PMCID: PMC3623375.

[43] Bhat KG, Khot P, Patil S, Pattar G, Majukar S. Antimicrobial susceptibility pattern of oral isolates of Aggregatibacter actinomycetemcomitans. J Oral Maxillofac Pathol. 2019 May-Aug;23(2):231-235. doi: 10.4103/jomfp.JOMFP_123_19. PMID: 31516229; PMCID: PMC6714249.

[44] Meto A, Colombari B, Sala A, Pericolini E, Meto A, Peppoloni S, Blasi E. Antimicrobial and antibiofilm efficacy of a copper/calcium hydroxide-based endodontic paste against Staphylococcus aureus, Pseudomonas aeruginosa and Candida albicans. Dent Mater J. 2019 Jul 31;38(4):591-603. doi: 10.4012/dmj.2018-252. Epub 2019 Jun 29. PMID: 31257304.

[45] Cutruzzolà F, Frankenberg-Dinkel N. Origin and Impact of Nitric Oxide in Pseudomonas aeruginosa Biofilms. J Bacteriol. 2016 Jan 1;198(1):55-65. doi: 10.1128/JB.00371-15. PMID: 26260455; PMCID: PMC4686190.

[46] Bassetti M, Vena A, Croxatto A, Righi E, Guery B. How to manage Pseudomonas aeruginosa infections. Drugs Context. 2018 May 29;7:212527. doi: 10.7573/dic.212527. PMID: 29872449; PMCID: PMC5978525.

[47] Thimmegowda U, Thomas J, Bilichodmath S, Preethi N. Identification of Specific Anaerobic Bacteria in Endodontic Infections of Primary Teeth-A PCR Study. Int J Clin Pediatr Dent. 2019 Jan-Feb;12(1):1-4. doi: 10.5005/jp-journals-10005-1573. PMID: 31496562; PMCID: PMC6710938.

[48] Brook I, Wexler HM, Goldstein EJ. Antianaerobic antimicrobials: spectrum and susceptibility testing. Clin Microbiol Rev. 2013 Jul;26(3):526-46. doi: 10.1128/CMR.00086-12. PMID: 23824372; PMCID: PMC3719496.

[49] Seguel, N, Quezada-Aguiluz, M, González-Rocha, G, Bello-Toledo, H & Sánchez-Sanhueza, G. Antibiotic resistance of Enterococcus faecalis from persistent endodontic infections. Int. J. Odontostomat., 2020;13(3):448-456.

[50] Barbosa FC, Irino K, Carbonell GV, Mayer MP. Characterization of Serratia marcescens isolates from subgingival biofilm, extraoral infections and environment by prodigiosin production, serotyping, and genotyping. Oral Microbiol Immunol. 2006 Feb;21(1):53-60. doi: 10.1111/j.1399-302X.2005.00254.x. PMID: 16390342.

[51] Fragkioudakis I, Tseleki G, Doufexi AE, Sakellari D. Current Concepts

on the Pathogenesis of Peri-implantitis: A Narrative Review. Eur J Dent. 2021 May;15(2):379-387. doi: 10.1055/s-0040-1721903. Epub 2021 Mar 19. PMID: 33742426; PMCID: PMC8184306.

[52] Premkumar A, Morse K, Levack AE, Bostrom MP, Carli AV. Periprosthetic Joint Infection in Patients with Inflammatory Joint Disease: Prevention and Diagnosis. Curr Rheumatol Rep. 2018 Sep 10;20(11):68. doi: 10.1007/s11926-018-0777-6. PMID: 30203376; PMCID: PMC6543529.

[53] Sun Y, Shu R, Li CL, Zhang MZ. Gram-negative periodontal bacteria induce the activation of Toll-like receptors 2 and 4, and cytokine production in human periodontal ligament cells. J Periodontol. 2010 Oct;81(10):1488-96. doi: 10.1902/jop.2010.100004. PMID: 20528699.

[54] Usui M, Onizuka S, Sato T, Kokabu S, Ariyoshi W, Nakashima K. Mechanism of alveolar bone destruction in periodontitis - Periodontal bacteria and inflammation. Jpn Dent Sci Rev. 2021 Nov;57:201-208. doi: 10.1016/j.jdsr.2021.09.005. Epub 2021 Oct 13. PMID: 34703508; PMCID: PMC8524191.

[55] Jividen G Jr, Misch CE. Reverse torque testing and early loading failures: help or hindrance? J Oral Implantol. 2000;26(2):82-90. doi: 10.1563/1548-1336(2000)026<0082:RTTAEL>2.3.CO;2. PMID: 11831335.