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### **REVIEWER'S REPORT**

Manuscript No.: IJAR-52487

Date: 26/06/2025

Title: Management of Peri-Implantitis: A Literature Review on Diagnosis, Therapy, and Long-Term Maintenance

Recommendation:	Rating	Excel.	Good	Fair	Poor
Accept as it is	Originality	•			
Accept after minor revisionYes	Tailar Oralit				
Accept after major revision	Techn. Quality	•			
Do not accept ( <i>Reasons below</i> )	Clarity		•		
	Significance		•		

Reviewer Name: Dr. Sireesha Kuruganti

Date: 26/06/2025

### **Reviewer's Comment for Publication.**

(To be published with the manuscript in the journal)

The reviewer is requested to provide a brief comment (3-4 lines) highlighting the significance, strengths, or key insights of the manuscript. This comment will be Displayed in the journal publication alongside with the reviewers name.

The manuscript provides a comprehensive literature review on the management of peri-implantitis, covering diagnosis, therapy, and long-term maintenance. It is well-structured and addresses a clinically relevant topic. The inclusion of emerging technologies and the CIST protocol adds significant value. The authors have synthesized a good amount of current evidence.

### **Detailed Reviewer's Report**

Here's an in-depth review of the manuscript, with observations and suggestions categorized for clarity. Overall Assessment:

The manuscript provides a comprehensive literature review on the management of peri-implantitis, covering diagnosis, therapy, and long-term maintenance. It is well-structured and addresses a clinically relevant topic. The inclusion of emerging technologies and the CIST protocol adds significant value. The authors have synthesized a good amount of current evidence.

Detailed Review with Line Numbers:

Abstract (Page 1)

\* Line 14-16: "Although implant-supported prostheses have achieved more than 90% long-term survival, prevalence of peri-implantitis continues to increase, with about 22% of patients developing the disease within a decade of implant placement." This statement effectively highlights the problem being addressed.

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\* Line 17-19: "The current evidence-based review literature discussed modern strategies for diagnosis, treatment, and long-term management of peri-implantitis." Clear statement of the review's purpose.

\* Line 20-22: "The disease is a multifactorial effect of interaction among microbial biofilms, host immune response, genetic susceptibility, and iatrogenic variables." This concisely summarizes the etiology.

\* Line 22-26: "Diagnosis is confirmed on the basis of a combination of clinical parameters and sophisticated modalities such as cone-beam computed tomography, MMP-8 biomarker assays, and microbial PCR analysis." Provides specific diagnostic methods.

\* Line 26-30: "Treatment depends on the stage of the disease: early peri-implantitis can be managed non- surgically by mechanical debridement, antiseptics, and lasers, whereas advanced disease most commonly requires resective or regenerative surgical interventions based on defect morphology." This is a good, concise overview of treatment approaches.

\* Line 30-32: "The Cumulative Interceptive Supportive Therapy (CIST) protocol is an evidence-based clinical strategy for intervention." Important to mention.

\* Line 32-35: "Emerging technologies such as antibacterial surface coatings, photodynamic therapy, and artificial intelligence augmented diagnostics have the potential to enhance clinical outcomes." Timely inclusion of newer advancements.

\* Line 35-38: "Yet, long-term success is dependent significantly on organized maintenance such as three-month recall visits, professional biofilm control, and radiographic surveillance." Emphasizes the crucial role of maintenance.

\* Line 38-41: "This review emphasizes the value of incorporating conventional and innovative therapies into a stage-specific, prevention-based model for optimizing peri-implant health and preventing implant loss." Good concluding statement for the abstract.

\* Line 41-43: Keywords are relevant and comprehensive.

Introduction (Page 1-2)

\* Line 34-40: "Dental implants have transformed oral rehabilitation with the provision of long-term, functional, and cosmetically acceptable solutions to tooth loss. With survival rates of more than 90% at 10 years, as determined by Pjetursson et al. (2012), implant-retained prostheses are now widely accepted worldwide as the gold standard for the replacement of missing teeth [1]." Strong opening establishing the importance of dental implants.

\* Line 40-42: "Their widespread global use is not only a sign of surgical progress but also patient satisfaction and long-term functional success." Good point on the broader impact.

\* Line 43-46: "But this therapeutic success comes at a biological price. Peri-implantitis, or inflammation of the peri-implant tissues followed by bone loss, has emerged as a major clinical problem around the practice of implant dentistry." Effectively sets up the problem of peri-implantitis.

\* Line 46-49: "While the disease can still remain undetected in its initial stages, its progression could be rapid and would eventually compromise the stability and survival of the implant." Highlights the insidious nature of the disease.

\* Line 49-53: "As noted by Smeets et al. (2014), peri-implantitis is a distinct clinical entity with a complex interrelation of risk factors that make both its diagnosis and treatment challenging [2]." Reinforces the complexity.

\* Line 53-56: "The burden of an epidemiological nature is high. Derks and Tomasi (2015) state that about 22% of patients develop peri-implantitis during a period of ten years post-implant placement." Provides critical epidemiological data.

\* Line 56-60: "Interestingly, patients with systemic risk factors-e.g., diabetes or smoking history-have a 3.2x greater chance of developing the disease, highlighting the need for patient selection and continuous risk evaluation [3]." Important for clinical practice.

\* Line 60-64: "In addition to its clinical implication, peri-implantitis also plays a huge economic impact. Salvi et al. (2017) indicated that the treatment of advanced lesions may cost as much as 350% higher than

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preventive treatment, often requiring complex retreatment or surgery [4]." The economic impact is a valuable addition.

\* Line 64-67: "Such repeated treatment can be detrimental to patient satisfaction, prolong healing, and diminish the perceived value of implant therapy." Good follow-up on the patient perspective.

\* Line 67-70: "Current research has highlighted the contribution of avoidable iatrogenic factors. Wilson (2009) identified the presence of residual cement, commonly unseen under the prosthetic margins, as being accountable for 81% of the initial cases of peri-implantitis [5]." This specific iatrogenic factor is a key takeaway.

\* Line 70-72: "This has generated renewed interest in careful prosthetic technique and careful observation after the placement." Highlights the clinical implication.

\* Line 72-76: "Microbiologically, the disease is most directly linked to specific pathogens that promote inflammatory breakdown. It has been shown through research that pathogens such as Porphyromonas gingivalis and Staphylococcus aureus have virulence factors that are capable of compromising host tissues and promoting inflammation within the peri-implant space [6]." Good detail on microbial factors.

\* Line 76-79: "While this microbial insult is not implant-specific, it appears to progress more quickly because of the absence of periodontal ligament defenses and the relatively compromised blood supply around the implant interface [2]." Explains the rapid progression around implants.

Aim of the Review (Page 2-3)

\* Line 70-74: "In light of these growing concerns, this literature review seeks to synthesize current clinical and scientific perspectives on peri-implantitis treatment." Clear objective.

\* Line 74-78: "It surveys current diagnostic methods, critically assesses non-surgical and surgical treatment options, and highlights the importance of early prevention, prosthetic planning, and long-term maintenance protocols." Comprehensive scope outlined.

\* Line 78-80: "Through the integration of evidence from landmark studies, this review offers clinicians a stage-specific, evidence-based strategy to minimize disease progression and enhance implant survival." Defines the benefit for clinicians.

Etiology and Pathogenesis (Page 3)

\* Line 83-85: "Peri-implantitis pathogenesis is a triad of factors: microbial colonization, host immune response, and biomechanical overload." Good summary of the contributing factors.

\* Line 85-87: "Natural teeth have a periodontal ligament that prevents pathogens from traveling freely along the implant-bone interface [2]." Provides a crucial distinction between natural teeth and implants.

\* Line 87-88: "Microbial Factors" - clear heading.

\* Line 89-91: "Gram-negative anaerobes prevail: Porphyromonas gingivalis has collagenases that break down connective tissue [6]." Specific bacterial examples are good.

\* Line 91-93: "Staphylococcus aureus in 28% of cases increases inflammation through lipoteichoic acid [7]." Adds further microbial detail.

\* Line 93-95: "Biofilms quickly develop on rough surfaces of titanium, particularly in microgaps at abutment connections [2]." Explains the vulnerability of implant surfaces.

\* Line 96-97: "Host Factors" - clear heading.

\* Line 98-99: "Smoking decreases tissue perfusion by 40% [10]." Provides a specific physiological impact.

\* Line 100-103: "Primary risk modulators are, Genetic susceptibility is polymorphisms like IL-1\beta+3953 and IL-1a-889, which have been reported to increase TNF- $\alpha$  production, enhancing susceptibility to peri-implant inflammation and bone loss [8]." Detailed genetic factors are valuable.

\* Line 103-105: "Systemic conditions: Diabetes (HbAlc>7%) affects neutrophil function [9]." Important systemic risk factor.

\* Line 106-107: "Iatrogenic Triggers" - clear heading.

\* Line 108-111: "Endoscopic study of failed implants supports the link between residual cement and 81% of early-onset peri-implantitis patients. [11]." Reiteration of a critical introgenic factor.

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\* Line 111-113: "Prosthetic design: Crowns that are overly contoured make it difficult to maintain proper hygiene [12]." Highlights another introgenic concern.

\* Line 113-114: "Occlusal overload occurs when excessive forces lead to bone resorption [13]." Completes the triad of iatrogenic factors.

Histopathological Perspective (Page 3)

\* Line 116-118: "Peri-implant lesions show more plasma cell infiltration compared to periodontitis, which accounts for their quicker progression (2.5 times faster bone loss) [2]." Provides a key histopathological distinction and explains faster progression.

Diagnostic Protocol (Page 3-4)

\* Line 119-123: "The clinical examination for peri-implantitis includes the use of plastic probes with a force of 0.25 N. The diagnostic criteria include detecting blood or pus while probing, probing depths of 6 mm or more, and movement, which implies a later stage of the illness [5]." Provides specific clinical diagnostic parameters.

\* Line 123-127: "The evaluation through radiographs involves standardised periapical images to measure bone loss, and cone-beam computed tomography (CBCT) is used to examine the three-dimensional shape of defects [14]." Details radiographic diagnostic methods.

\* Line 127-130: "Advanced diagnostics feature MMP-8 point-of-care tests, providing 89% sensitivity in predicting active bone loss [15], alongside microbial PCR testing that reveals pathogen profiles for more precise antibiotic therapy [16]." Mentions advanced diagnostic tools and their benefits.

\* Line 130-133: "It's important to remember that obtaining baseline radiographs when loading a prosthetic is crucial. If bone loss surpasses 0.2 mm per year from this initial point, it suggests the presence of a problem [17]." Emphasizes the importance of baseline and quantifiable changes. Non-Surgical Therapy (Page 4)

\* Line 135-137: "For early peri-implantitis and mucositis with probing depths of 5 mm or less, first-line therapy is recommended." Defines the scope of non-surgical treatment.

\* Line 137-138: "Jepsen and colleagues (2015) emphasise that managing mechanical plaque is still essential [18]." Highlights the foundational aspect of plaque control.

\* Line 138-143: "Key methods include erythritol air-polishing, which reduces biofilm by 67% at a 60° angle [19], using titanium curettes to remove calculus without harming implant surfaces, and using ultrasonics with PEEK-coated tips in conjunction with glycine irrigation." Provides specific non-surgical techniques and their efficacy.

\* Line 143-147: "Adjunctive therapy includes local antiseptics using chlorhexidine chips, which prevent infections for 21 days [20] and systemic antibiotics, especially amoxicillin-metronidazole (500 mg TID for 7 days), for severe cases [21]." Details adjunctive therapies.

\* Line 147-148: "With a 2940 nm wavelength, the Er:YAG laser destroys 89% of biofilm [22]." Mentions laser therapy and its effectiveness.

\* Line 149-152: "Nonetheless, non-surgical treatment has its limitations, achieving resolution in only 37% of pockets exceeding 5 mm because of threads that are difficult to access [23]." Acknowledges limitations, which is important for a balanced review.

Surgical Management (Page 4)

\* Line 154-158: "Reconstructive surgery is recommended for horizontal defects [24] and involves techniques including osteoplasty to produce positive architecture, implantoplasty with diamond burs to smooth exposed threads, and an apically positioned flap." Describes resective techniques.

\* Line 158-160: "At three years, results indicate a 72% disease remission rate, despite the absence of bone fill [25]." Provides outcome data for resective surgery.

\* Line 160-165: "During regenerative surgery, which follows the gold standard procedure [26], flap elevation and degranulation, surface decontamination with an Er:YAG laser, application of a xenograft (DBBM) combined with a collagen membrane, and primary closure are all steps that are taken." Details the steps of regenerative surgery.

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\* Line 165-167: "Results show that 81% of bone had filled in by the 24-month mark [27]." Provides outcome data for regenerative surgery.

\* Line 167-171: "In a recent study, Roccuzzo et al. (2024) demonstrated that the combination of bone grafts and platelet-rich fibrin (PRF) not only accelerates the process of angiogenesis but also cuts the amount of time needed for healing by 35 percent [28]." Highlights a very recent and relevant finding. Clinical Considerations and Maintenance (Page 4-5)

\* Line 173-176: "One important consideration for choosing the right treatment is the morphology of the peri-implant defect. With a reported success rate of 81% [27], regenerative methods are most suited for treatments that involve abnormalities with three or four walls." Emphasizes defect morphology as a key decision factor.

\* Line 176-179: "A combination of regenerative procedures and guided bone regeneration (GBR) is effective in treating crater-shaped lesions, with a 68% success rate." Provides specific success rates for different defect types.

\* Line 179-181: "Resective surgery is the most effective way to treat horizontal abnormalities, with a 72% success rate [25]." Further details on treatment selection based on morphology.

\* Line 181-182: "Decontamination of the implant surface is another essential component towards achieving excellent outcomes." Crucial step highlighted.

\* Line 182-186: "Considered the gold standard due to its 98% bacterial kill rate, the Er:YAG laser is Chemical agents including 24% EDTA gel [30] can effectively remove endotoxin from the implant surface." Details methods for surface decontamination.

\* Line 186-189: "Consequently, it is imperative to avoid damaging or changing the surface of the implant by not utilising metal curettes during the cleaning procedure." Important clinical caution.

\* Line 189-191: "Supportive maintenance is essential in preventing the recurrence of peri-implantitis. Jepsen et al. (2015) emphasised that implementing a structured recall every three months can lead to a 58% reduction in recurrence rates [18]." Strong emphasis on maintenance and supporting data.

\* Line 191-194: "During maintenance visits, clinicians are required to evaluate probing depths (PD), bleeding on probing (BoP), and the mobility of implants." Specific parameters for maintenance visits.

\* Line 194-196: "Re-instrumentation generally involves the application of air-polishing in conjunction with titanium curettes." Details re-instrumentation techniques.

\* Line 196-198: "It is recommended that high-risk patients receive antimicrobial support, such as 0.12% chlorhexidine rinses." Specific recommendation for high-risk patients.

\* Line 198-200: "Annual periapical radiographs are recommended to assess bone levels and identify early changes." Important for long-term monitoring.

\* Line 200-203: "Long-term outcomes indicate that survival rates are significantly higher with supportive care, achieving 92.3% at five years with regular maintenance, in contrast to 64.7% without such care. [31]" Provides compelling evidence for the value of maintenance.

Figure 1 (Page 5)

\* Line 64 (Image): The conceptual figure is highly valuable. It provides a clear visual decision tree for peri-implantitis management based on defect morphology. The timeline diagram is also very helpful for understanding progression and intervention points.

\* Line 144-148 (Legends): The legends clearly explain the components of Figure 1 and appropriately cite the sources from which the data was adapted.

Emerging Innovations (Page 5-6)

\* Line 77-78: "New technologies are playing an important role in the management of peri-implantitis." Good transition.

\* Line 78-80: "Antibacterial coatings using zinc oxide nanoparticles show promise in reducing microbial adhesion on implant surfaces [32]." Specific emerging technology.

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\* Line 80-82: "Photodynamic therapy, using methylene blue combined with 660 nm wavelength light, shows promise for the eradication of pathogenic microorganisms [33]." Another relevant emerging therapy.

\* Line 82-87: "The diagnosis accuracy of peri-implant bone loss detection has been much enhanced by the use of artificial intelligence, most especially by convolutional networks. The stated general accuracy spans 61% to 94.74%. Early and accurate detection of peri-implant illness enabled by these artificial intelligence models helps doctors enhance the results and planning of treatment. [34]." AI in diagnostics is a significant and cutting-edge inclusion.

Clinical Protocol: The CIST Framework (Page 6-7)

\* Line 88-92: "From the clinical presentation, the Cumulative Interceptive Supportive Therapy (CIST) protocol, developed by Lang and Berglundh [35], is a structured, phase-oriented approach for the treatment of peri-implant disease." Clearly introduces the CIST protocol.

\* Line 92-94: "Throughout treatment, it allows for timely intervention at every level, ranging from the initial mucosal inflammation to the late stages of bone loss." Highlights the benefit of the CIST protocol.

\* Line 85 (Table): The table presenting the CIST framework is excellent. It provides a concise and clear breakdown of stages, clinical presentations, interventions, and key references. This is a very strong element of the review.

\* Line 86-88: "As an example, a diabetic patient who presents with a probing depth of 6 millimetres and a bone loss of 3 millimetres is considered to be in Stage C. Because of this particular circumstance, the intervention that would be most suitable would be mechanical debridement in conjunction with minocycline microspheres [36]." Provides a practical example of applying the CIST protocol.

\* Line 87-88: The reference [36] is provided at the end of the sentence.

\* Line 88-90: "Later, if the problem doesn't go away, Stage D treatment would be done, which includes access flap surgery, decontamination with an Er:YAG laser, and the use of a xenograft with platelet-rich fibrin (PRF) [28]." Continues the practical example to Stage D, showing the progression of treatment. Conclusion (Page 7)

\* Line 92-94: "Peri-implantitis has a higher prevalence and clinical severity, thus it requires a systematic, evidence-based diagnosis, intervention, and maintenance." Strong opening summarizing the importance of the topic.

\* Line 94-97: "Early diagnosis with diagnostic tools such as MMP-8 testing and initial x-rays is essential to enable physicians to observe when the disease progresses in a timely way." Reaffirms the importance of early diagnosis.

\* Line 97-99: "Treatment should be led by defect morphology; non-surgical interventions are acceptable for early disease, while regenerative treatments are ideal for contained abnormalities." Reinforces treatment selection based on defect morphology.

\* Line 99-102: "Structured maintenance, involving recalls every quarter, has been shown to decrease recurrence by 58% [18], underlining the importance of long-term follow-up."