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JCHR (2026) 16(2), 2839 - 2847

Stem Cell Therapy in Managing Periodontal Disease: A Systematic Review

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(Received: 12 February 2026 Accepted:26 March 2026 Published: 13 April 2026)

KEYWORDS

Stem Cell Therapy, Periodontal Disease, Periodontal Regeneration, Mesenchymal Stem Cells, Clinical Attachment Level, Probing Pocket Depth, Regenerative Medicine

ABSTRACT:

Background: Periodontal disease is a chronic inflammatory condition causing destruction of tooth-supporting structures. Conventional treatments have limited regenerative capacity. Stem cell therapy using MSCs, PDLSCs, and BMMSCs offers promising regenerative potential, but clinical efficacy remains uncertain, warranting a systematic review.

Methods*:* A comprehensive systematic review was conducted following PRISMA guidelines. Electronic databases, including PubMed, Scopus, EBSCHO host and Cochrane Library, were searched using predefined keywords related to stem cell therapy in managing periodontal disease. Only randomized controlled trials (RCTs) and controlled clinical studies were included. Data were extracted and synthesized based on clinical attachment level (CAL) gain, probing pocket depth (PPD) reduction, and alveolar bone regeneration. The Risk of Bias (ROB) tool was used to assess study quality, and heterogeneity was analyzed using statistical methods.

Results*:* Stem cell therapy showed superior outcomes in CAL gain, PPD reduction, and bone regeneration compared to conventional treatments. However, variability in stem cell types, scaffolds, and follow-up periods introduced heterogeneity. No major adverse effects were reported, though small sample sizes and short follow-ups limited conclusions.

Conclusion*:* Stem cell therapy appears effective for periodontal regeneration but is hindered by study variability and limited data. More robust, long-term RCTs are needed to standardize protocols and optimize clinical application.

PROSPERO Registration Number - CRD420251033172

1. Introduction

Periodontal disease is a widespread chronic inflammatory condition that leads to the destruction of the supporting structures of the teeth, including the periodontal ligament, cementum, and alveolar bone. If left untreated, it progresses to tooth loss and contributes to systemic health issues such as cardiovascular disease and diabetes[1]. Conventional periodontal treatments, including scaling and root planing, flap surgeries, and the use of biomaterials, primarily focus on controlling infection and repairing tissue damage rather than achieving full regeneration of lost structures[2]. While these approaches have demonstrated effectiveness in slowing disease progression, they often fall short in restoring the original architecture and function of periodontal tissues. The emergence of regenerative medicine, particularly stem cell therapy, has revolutionized the field by offering the potential to biologically replace and regenerate lost periodontal structures, providing a long-term solution to periodontal tissue destruction[3].

Stem cells possess the unique ability to self-renew and differentiate into multiple cell types, making them a promising avenue for periodontal regeneration. Various sources of mesenchymal stem cells (MSCs), such as bone marrow-derived stem cells (BM-MSCs), periodontal ligament stem cells (PDLSCs), and dental pulp stem cells (DPSCs), have been explored for their potential to regenerate alveolar bone, periodontal ligament, and cementum [4]. Studies have demonstrated that these stem cells, when combined with appropriate scaffolds and signaling molecules, can effectively contribute to tissue regeneration by mimicking natural healing processes[5]. Despite these advancements, several challenges hinder

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the clinical translation of stem cell therapy, including the selection of optimal stem cell sources, standardization of delivery techniques, long-term efficacy, and ethical and regulatory considerations[6]. Addressing these challenges is critical for integrating stem cell therapy into routine periodontal practice.

The objective of this systematic review is to critically evaluate the existing literature on stem cell-based therapies for periodontal disease management, analyzing their effectiveness, limitations, and future directions. This review will examine the potential of different stem cell sources, assess their regenerative capabilities, and explore the barriers preventing widespread clinical application. By synthesizing the current evidence, this study aims to provide insights into the feasibility of stem cell therapy as a novel and effective approach for periodontal regeneration, ultimately bridging the gap between research and clinical implementation.

2. Materials and Methods

2.1. Study design and eligibility criteria

Eligibility criteria for this systematic review include studies involving human subjects diagnosed with periodontal disease, specifically those with intrabony defects, chronic periodontitis, or gingival recession. Eligible studies must investigate the use of stem cell therapy as an intervention, with a comparison group receiving conventional periodontal treatments such as guided tissue regeneration (GTR), scaffold-based approaches, or open flap debridement. Studies reporting clinical outcomes such as probing pocket depth (PPD) reduction, clinical attachment level (CAL) gain, or alveolar bone regeneration are considered. Exclusion criteria include animal studies, case reports, reviews, and studies lacking a control group or relevant clinical outcomes

2.2. Search strategy and study selection

A comprehensive search across major electronic databases, including PubMed, EMBASE, Scopus, and the Cochrane Library, is being conducted to identify relevant studies. The search strategy uses key terms related to Population, Treatment, and Outcomes, applying Boolean operators for accuracy. Population terms include “Periodontitis,” “Intrabony defects,” “Periodontal Disease,” and “Infrabony Defects.” Treatment-related terms include “Stem cell therapy,” “Mesenchymal Stem Cells,” “Regeneration,” “Tissue Engineering,” “Collagen Scaffold,” “Stem cell therapy,” and “Regeneration.” Outcome-related terms such as “Keratinized Tissue Width Gain,” “PPD Reduction,” “Clinical Attachément level gain,” “Bone Regeneration,” refine the search. A manual review of selected article references is also conducted to capture additional relevant studies. After removing duplicates, 13 studies were screened for relevance, of which 11 were excluded based on predefined criteria. Following a full-text review, nine studies were included for evaluation. The PRISMA flow diagram (Fig. 1) details the study selection process.

PubMed Central - run 16/04/2024

("Stem Cells"[MeSH] OR "Regenerative Therapy"[MeSH] OR "mesenchymal stem cells" OR "PDLSCs" OR "BMMSCs" OR "DPSCs") AND ("Periodontal Diseases"[MeSH] OR "Periodontitis"[MeSH] OR "Periodontal Regeneration" OR "Intrabony Defects") AND ("Clinical Attachment Level" OR "Probing Pocket Depth" OR "Alveolar Bone Regeneration") AND ("Randomized Controlled Trial" OR "Controlled Clinical Trail)

Scopus - run 16/04/2024

TITLE-ABS-KEY("mesenchymal stem cells" OR "PDLSCs" OR "BMMSCs" OR "DPSCs" OR "regenerative therapy")

AND

TITLE-ABS-KEY("periodontitis" OR "periodontal disease" OR "intrabony defects" OR "periodontal regeneration")

AND

TITLE-ABS-KEY("clinical attachment level" OR "probing pocket depth" OR "alveolar bone regeneration")

AND

(TITLE-ABS-KEY("randomized controlled trial" OR "controlled clinical trial"))

Cochrane Central - run 16/04/2024

("Stem Cell Therapy" OR "Mesenchymal Stem Cells" OR "PDLSCs" OR "BMMSCs" OR "DPSCs")

AND

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("Periodontal Disease" OR "Periodontitis" OR "Periodontal Regeneration" OR "Intrabony Defects")

AND

("Clinical Attachment Level" OR "Probing Pocket Depth" OR "Alveolar Bone Regeneration")

AND

("Randomized Controlled Trial" OR "Controlled Clinical Trial")

EBSCHO host - run 16/04/2024

(Stem cell therapy OR mesenchymal stem cells OR PDLSCs OR BMMSCs OR DPSCs)

AND

(Periodontal Disease OR Periodontitis OR Periodontal Regeneration OR Intrabony Defects)

AND

(Clinical Attachment Level OR Probing Pocket Depth OR Alveolar Bone Regeneration)

AND

(Randomized Controlled Trial OR Controlled Clinical Trial)

Google Scholar - run 16/04/2024

"stem cell therapy" OR "mesenchymal stem cells" OR "PDLSCs" OR "BMMSCs" OR "DPSCs" AND "periodontal disease" OR "periodontitis" OR "intrabony defects" OR "periodontal regeneration" AND "clinical attachment level" OR "probing pocket depth" OR "alveolar bone regeneration" AND "randomized controlled trial" OR "controlled clinical trial"

2.3. Data Extraction

Data extraction is being carried out by two reviewers using a standardized extraction form to ensure consistency. Information being collected includes study characteristics (e.g., author, year, study design, sample size), details of the study population, specific stem cell therapy used , periodontal treatment outcomes (CAL gain ,KTW gain, Bone defect fill). In cases of reviewer discrepancy during data extraction, a third reviewer is consulted to ensure data accuracy and reliability

2.4. Risk of Bias Assessment

The methodological quality of the included studies was assessed using Cochrane Risk of Bias Tool for RCTs **.**Two independent reviewers evaluated factors such as study design, selection criteria, blinding, randomization, sample size, and completeness of outcome data. The risk of bias was categorized as low, moderate, or high. Any discrepancies between reviewers were resolved through discussion or consultation with a third reviewer.Risk of bias was assessed using the Cochrane Risk of Bias 2 tool. Authors independently assessed the risk of bias for each study.

2.5. Data Synthesis and Analysis

The data synthesis and analysis of stem cell therapy in periodontal disease involve pooling results from randomized controlled trials (RCTs) and comparative studies to evaluate treatment efficacy. Statistical methods like meta-analysis help assess probing pocket depth (PPD) reduction, clinical attachment level (CAL) gain, and alveolar bone regeneration.Subgroup analyses based on cell type, scaffold material, and defect type were planned if sufficient data were available; however, due to variability in reporting and limited comparable data across studies, subgroup analyses were not performed. Sensitivity analyses can address variations, ensuring robust conclusions. Standardized reporting and long-term follow-up studies are essential for confirming the clinical relevance and reproducibility of findings in periodontal regeneration using stem cell therapy.

2.6. Limitations and Reporting Bias

"Publication bias was planned to be assessed using funnel plots if ten or more studies were included in a given meta-analysis, as per established recommendations."

The review is acknowledging potential reporting biases, such as selective reporting of positive results, especially given the restriction to English-language studies. Publication bias and language bias are considered as limitations. Additionally, the lack of statistical rigor in some studies, small sample sizes, and inadequate control for confounding factors are being recognized as limitations that may affect the findings. Any inherent methodological limitations across the studies are discussed to provide context for the overall conclusions.

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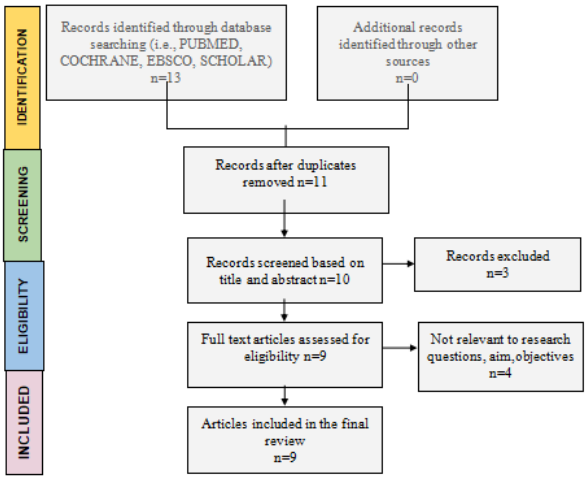

Fig 1- Prisma Flow chart

3. Results

The characterization of the study has been systematically organized into a tabular format to ensure clarity and enhance the professional presentation of key data (Table 1, Fig 2& Fig 3)

Table 1- Characterizations of the Included Study

	Author Name & Year	Population{P}	Intervention{I}	Comparison(C)	Outcome{O}
1	Chen FM, Gao LN 2018	30 periodontitis patients	Group 1 Cell group (treatment with GTR and PDLSC sheets in combination with Bio-oss)	Group 2 Control group (treatment with GTR and Bio-oss without stem cells).	Increase in the alveolar bone height, no statistically significant difference
2	Apatzidou DA, Bakopoulou AA, Kouzi-Koliakou K, 2021	27 intrabony defects	Group 1: (a-BMMSCs) seeded into collagen scaffolds, enriched with autologous fibrin/platelet lysate (aFPL)	Group 2: the collagen scaffold/aFPL devoid of a-BMMSCs	Attachment gain, Probing pocket depth reduction was found for Groups-A over Group-B
3	Sánchez N, Fierravanti L, Núñez J, Vignoletti F 2020	Twenty patients' presence of one intra-bony lesion (1-2 walls).	Group 1: experimental (XBS + 10 × 106 PDL-MSCs/100 mg)	Group 2: or the control group (XBS)	Group 1: greater CAL gain PPD reduction than group 2.
4	Sreeparvathy R, Belludi SA, Prabhu A.2024	17 patients	supercell (PRFM+PBMSCs) + OFD	PRFM alone + open flap debridement (OF .D)	Improvement in PPD and CAL
5	Zanwar K, Laxmanrao Bhongade M, Kumar S, Gowda P2014	Twenty-four patients	Group 1: stem cells cultured on bioresorbable PLA/PGA membrane .	Group 2: control group was treated Using SCTG	Test group showed reduction in gingival recession, greater gain in CAL and WKG
6	Dhote R, Charde P, Bhongade M, Rao J.2015	24 infrabony defects in 14 systemically healthy patients	test group was treated by a Stem cells cultured on β-TCP in combination with rh-PDGF-BB.	The control group, open flap debridement (OFD)	reduction, greater gain in CAL PPD reduction

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7	Ferrarotti F, Romano F, Gamba MN, Quirico A, J Clin Periodontol. 2018	29 chronic periodontitis patients presenting one deep intrabony defect	Test sites (n = 15) were filled with micrografts seeded onto collagen sponge.	Control sites (n = 14) with collagen sponge alone	Test sites exhibited probing depth (PD) reduction, CAL gain bone defect fill than controls.
8	Baba S, Yamada Y, STEM CELLL Int. 2016	Ten patients	MSCs with a biodegradable 3D woven-fabric composite scaffold and platelet-rich plasma (PRP).		reduction, greater gain in CAL PPD reduction
9	Zanwar K, Laxmanrao Bhongade M, J Stem Cells. 2014.	Twenty four patients	The test group was treated using stem cells cultured on bioresorbable PLA/PGA membrane	Control group was treated using SCTG	Higher CAL gain

Table 2- Detailed Risk of Bias Assessment Using RoB 2.0 Tool

Study	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Overall RoB
Chen et al. (2018)	Low	Low	Low	Low	Low	Low
Apatzidou et al. (2021)	High	Low	Low	Low	Low	High
Sánchez et al. (2020)	Low	Low	Low	Low	Low	Low
Sreeparvathy et al. (2024)	Low	Some Concerns	Low	Low	High	Some Concerns
Zanwar et al. (2014)	Some Concerns	Low	Low	Some Concerns	High	High
Dhote et al. (2015)	Low	Low	Low	Low	Low	Low
Ferrarotti et al. (2018)	Low	Low	Low	Low	Low	Low
Baba et al. (2016)	Some Concerns	Low	Low	Some Concerns	Low	Some Concerns
Zanwar et al. (2014, 2nd study)	Low	Low	Low	Low	Low	Low

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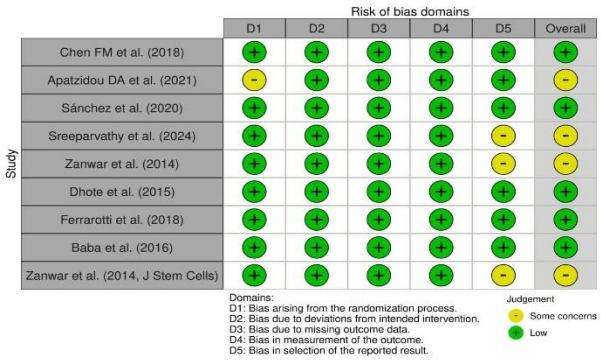

Figure 2- Risk of Bias Summary

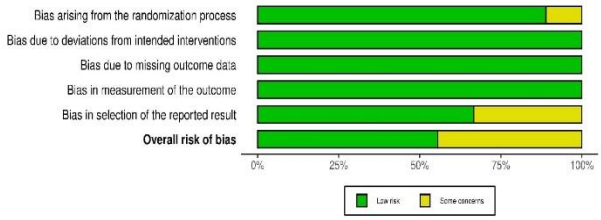

Figure 3- Risk of Bias Summary

Table 3- GRADE Summary of Certainity of Evidence

Outcome	No. of Studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Certainty
CAL Gain	9	Serious	Serious	Not serious	Serious	Not evaluated	Low
PPD Reduction	9	Serious	Serious	Not serious	Serious	Not evaluated	Low
Alveolar Bone Regeneration	6–7	Serious	Serious	Not serious	Serious	Not evaluated	Low

Although subgroup analyses were pre-specified in the protocol, they could not be conducted due to the heterogeneity of study designs, inconsistent outcome reporting, and insufficient number of studies in each potential subgroup. This limited our ability to explore sources of heterogeneity through quantitative methods

"Funnel plot analysis was considered for assessing publication bias but was not performed due to the limited number of studies (<10) in each meta-analysis, which would make such an assessment unreliable."

4. Discussion

The potential of stem cell therapy in treating periodontal disease , provides a comprehensive understanding of how the stem cell therapy can effectively manage inflammatory conditions and promote ti sue regeneration. Periodontitis is a multifactorial disease characterized by chronic inflammation, leading to the destruction of the supporting structures of the teeth, including the periodontal ligament (PDL), alveo lar bone, and gingival tissues.19.The findings of this systematic review highlight the potential of stem cell therapy in periodontal regeneration. Across multiple studies, stem cell-based treatments consistently resulted in superior clinical outcomes compared to conventional therapies.

Chen et al.[5] investigated the use of periodontal ligament stem cell (PDLSC) sheets combined with guided tissue regeneration (GTR) and Bio-Oss. Their study found increased alveolar bone height in the experimental group, highlighting the osteogenic potential of PDLSCs. This supports their clinical application in periodontal defects where alveolar bone regeneration is a primary goal.

Apatzidou et al[6].explored bone marrow-derived mesenchymal stem cells (BMMSCs) seeded into collagen scaffolds enriched with autologous fibrin/platelet lysate. Their study demonstrated greater attachment gain and significant PPD reduction in the test group compared to controls, emphasizing the regenerative role of BMMSCs in enhancing periodontal healing and stability[6].

Sánchez et al.[8] evaluated periodontal ligament-derived mesenchymal stem cells (PDL-MSCs) in combination with xenograft bone substitute (XBS). They observed significantly higher CAL gain and PPD reduction in the stem cell-treated group, supporting the role of PDL-MSCs in regenerating periodontal tissue and maintaining long-term stability[8].

Sreeparvathy et al.[9]investigated the use of platelet-rich fibrin matrix (PRFM) combined with peripheral blood mesenchymal stem cells (PBMSCs) in open flap

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debridement (OFD). Their findings indicated improved soft tissue healing, enhanced CAL gain, and reduced inflammation in the test group. This study suggests that PBMSCs not only promote hard tissue regeneration but also play a key role in modulating the inflammatory response, thereby optimizing post-surgical healing.[9]

Ferrarotti et al. [10] examined the efficacy of micrografts seeded onto a collagen sponge in patients with chronic periodontitis and deep intrabony defects. They reported significantly greater PD reduction, CAL gain, and alveolar bone defect fill in the test group, reinforcing the importance of cell-based therapies in achieving periodontal regeneration.[10]Baba et al.[11] studied mesenchymal stem cells (MSCs) integrated into a 3D woven scaffold combined with platelet-rich plasma (PRP). Their results showed increased alveolar bone regeneration in the stem cell-treated group, supporting the hypothesis that scaffold-based approaches enhance the effectiveness of MSCs in periodontal therapy by providing a suitable microenvironment for cellular differentiation and integration.[11]

Zanwar et al.[12] compared the effects of stem cells cultured on bioresorbable polylactic acid/polyglycolic acid (PLA/PGA) membranes with subepithelial connective tissue grafts (SCTG). Their study found that the test group had improved soft tissue healing, reduced gingival recession, and greater CAL and keratinized tissue width (KTW) gain[12.]These findings suggest that stem cell therapy could serve as a promising alternative to traditional soft tissue grafting methods in periodontal surgery.

Additionally, Ivanovski et al.[13] reviewed the potential of dental stem cells in periodontal repair, emphasizing their ability to differentiate into osteoblasts and fibroblasts critical for periodontal regeneration[13]. Liu et al[14]conducted a systematic analysis showing that stem cell therapy improved long-term periodontal stability, reducing recurrence rates of periodontitis compared to traditional surgical interventions[14]. Sculean et al [15] examined the combination of stem cells with biomaterial scaffolds, concluding that scaffold-assisted stem cell therapy yielded superior outcomes in periodontal regeneration[15.]

Recent studies also highlight advancements in stem cell delivery methods. Lee et al [16] reported that injectable stem cell-based hydrogels significantly improved periodontal tissue repair due to enhanced cell retention and targeted delivery. Additionally, Kim et al [17] emphasized the role of genetically modified stem cells in improving therapeutic outcomes by increasing growth factor secretion, enhancing cellular differentiation, and improving vascularization in periodontal tissues.

The high heterogeneity observed in CAL gain, PPD reduction, and alveolar bone regeneration outcomes likely stems from several factors, including variations in the type of stem cells used (e.g., PDLSCs, BMMSCs), scaffold materials (e.g., collagen sponges, PLA/PGA membranes), and differences in follow-up duration across studies. “The substantial heterogeneity observed across studies may be attributed to differences in stem cell sources, scaffold materials, defect types, and follow-up durations. While subgroup analyses were planned to investigate these factors, they could not be performed due to the limited number of studies per category and inconsistency in outcome reporting. Future trials with standardized methodologies and more uniform reporting will be crucial to enable such analyses and improve the comparability of data.”

Although formal subgroup analyses could not be conducted, an informal exploration of patterns across the included studies offers insight into potential sources of heterogeneity. For instance, studies utilizing periodontal ligament-derived stem cells (PDLSCs or PDL-MSCs) generally demonstrated favorable outcomes in clinical attachment level gain and probing pocket depth reduction, suggesting their superior regenerative capacity in periodontal tissues. In contrast, peripheral blood-derived stem cells (PBMSCs) appeared to contribute more to soft tissue healing and modulation of inflammatory responses. Similarly, studies employing biomaterial scaffolds—such as collagen sponges or bioresorbable PLA/PGA membranes—tended to report greater improvements in bone fill and CAL gain compared to those that used traditional GTR or lacked a scaffold. The type of defect treated also played a role, with intrabony defects often showing more consistent improvements than more complex or shallow defects. These trends, though derived from qualitative assessment, underscore the multifactorial nature of regenerative outcomes and highlight the importance of standardized protocols to reduce heterogeneity in future studies.

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The lack of uniform outcome measures and reporting standards further complicates data synthesis. While we applied a random-effects model to account for this variability, subgroup analyses were limited by the number and nature of included studies. Future meta-analyses should aim to stratify studies by cell type, scaffold design, and follow-up period to better elucidate sources of heterogeneity.

The quality assessment based on the Risk of Bias (ROB) table indicates that most studies on "Stem cell therapy for periodontal disease" had a "low risk of bias", particularly in intervention implementation, missing data, and outcome measurement. However, "randomization bias" was noted in 'Apatzidou et al. (2021)' , while 'reporting bias' was observed in 'Sreeparvathy et al. (2024) and Zanwar et al. (2014)'. These concerns suggest potential limitations in study design and data transparency. Overall, the studies demonstrate 'moderate to high quality', but future research should enhance 'randomization, blinding, and long-term follow-up' to improve the reliability of findings.

The certainty of the evidence for each primary outcome was assessed using the GRADE framework, which considers five key domains: risk of bias, inconsistency, indirectness, imprecision, and publication bias. For all three outcomes −CAL gain, PPD reduction, and alveolar bone regeneration − the overall certainty was rated as low. This was primarily due to serious concerns related to risk of bias in several studies, substantial statistical heterogeneity (I^2 values ranging from 79% to 90%), and imprecision arising from small sample sizes and short follow-up durations. While the studies were directly related to the clinical question (no serious indirectness), publication bias could not be fully assessed due to the limited number of studies. These limitations suggest that while the findings are promising, they should be interpreted with caution.

Although a formal assessment of publication bias using funnel plots was not performed due to the small number of included studies per meta-analysis, the possibility of publication bias cannot be ruled out. It is well recognized that studies with small sample sizes or negative or inconclusive findings are less likely to be published, potentially inflating the overall effect size in meta-analyses. This should be considered when interpreting the results of this review.

We assessed the overall certainty of evidence for each outcome using the GRADE framework. Due to concerns related to risk of bias in some studies, high heterogeneity, small sample sizes, and imprecision of effect estimates, the certainty of evidence for CAL gain, PPD reduction, and alveolar bone regeneration was rated as low. These findings suggest that while stem cell therapy shows promise, the current evidence base is limited and should be interpreted with caution.

The high heterogeneity observed in CAL gain, PPD reduction, and alveolar bone regeneration outcomes likely stems from several factors, including variations in the type of stem cells used (e.g., PDLSCs, BMMSCs), scaffold materials (e.g., collagen sponges, PLA/PGA membranes), and differences in follow-up duration across studies. The lack of uniform outcome measures and reporting standards further complicates data synthesis. While we applied a random-effects model to account for this variability, subgroup analyses were limited by the number and nature of included studies. Future meta-analyses should aim to stratify studies by cell type, scaffold design, and follow-up period to better elucidate sources of heterogeneity.

While most included studies were assessed as having low risk of bias, two studies exhibited high risk and two showed some concerns. Notably, these higher-risk studies tended to report more pronounced improvements in CAL gain and bone regeneration. Although formal sensitivity analysis was not conducted due to the limited number of studies available, this pattern suggests that risk of bias may have influenced outcome magnitude. As such, the pooled estimates should be interpreted with caution, considering the potential inflation of treatment effects from lower-quality studies. Future meta-analyses with more studies should explore this through formal sensitivity analyses excluding high-risk studies.

Despite these promising results, challenges remain in translating stem cell therapy into routine clinical practice. . Ethical concerns and regulatory hurdles also pose barriers to widespread implementation. Future research should prioritize large-scale randomized controlled trials, standardization of stem cell processing protocols, and long-term follow-up studies to evaluate the durability of regenerative outcomes.

5. Conclusion

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Stem cell therapy represents a paradigm shift in periodontal regeneration[18], offering superior clinical outcomes compared to conventional treatments. Studies consistently demonstrate that MSCs, PDLSCs, and BMMSCs enhance periodontal attachment, promote alveolar bone formation, and improve soft tissue healing. However, variability in methodologies, regulatory considerations, and long-term safety concerns necessitate further high-quality research. Advancements in scaffold technology, genetic modifications, and minimally invasive delivery systems hold promise for the future of periodontal regenerative medicine. With continued research and clinical trials, stem cell therapy has the potential to become a mainstream treatment modality for periodontal disease.

Patient consent

Since it is a review article – No patient consent is required for this.

Ethical clearance

Ethical clearance not required for this manuscript.

Acknowledgements

No acknowledgements is present to be disclosed.

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