Case Report

Morphometric Assessment of Mesenchymal Stem Cell Therapy in Augmentation of Posterior Mandibular Ridge

Ola Mahmoud Zayed [1], Ashraf Fathy [2],Saher Sayed Mohammed [3], Hala Gabr Metwally Sayed Ahmed [4],Fadwa Elshenawy Atteya Elshenawy [5]

[1] *MSc, Tanta University (2015) Faculty of Dentistry, Minia University,*
[2] *Professor of Oral and Maxillofacial SurgeryFaculty of Dentistry, Minia University,*
[3] *Head of Oral Biology Department Faculty of Dentistry, Minia University,*
[4] *Professor of Clinical and Chemical Pathology Faculty of Medicine, Cairo University*
[5] *Demonstrator at Oral medicine and periodontology , Faculty of Dentistry, Alsalam University*

ABSTRACT

Alveolar ridge deficiencies, particularly of the posterior mandible, are extremely difficult to rehabilitate with implant and other functional restoration. Vertical bone augmentation in this area is typically indicated to ensure an adequate anchorage of the implant and long-term stability. While traditional bone grafting techniques, i.e., the use of xenografts and platelet-rich fibrin (PRF), have also provided promising outcomes, the use of mesenchymal stem cells (MSCs) may contribute to bone healing by stimulating cellular activity and promoting osteogenesis [1,2].MSCs derived from Wharton's Jelly, due to their inbuilt high rate of proliferation and ability to undergo differentiation towards the osteogenic lineage, provide a novel dimension to the engineering of bone tissue[3]. This study will compare the efficacy of the application of xenograft and PRF with Wharton's Jelly-derived MSCs for vertical bone augmentation of the posterior mandible against the efficacy of the application of xenograft and PRF,which will offer greater predictability and long-term outcomes in implant-supported rehabilitation of compromised mandibular ridges[4]. Methods: Five female patients aged between 45 and 55 years were chosen and divided randomly into two groups in a split-mouth design. Group 1 is vertical bone augmentation using xenograft and PRF, while Group 2 is a combination of xenograft, PRF, and MSCs derived from Wharton's Jelly on the other side. Inclusion criteria were patients who have a minimum of 5 mm depth of alveolar ridge defect and 2.8 mm width in the posterior mandible and overall good health and compliance during follow-ups. Exclusion criteria were systemic diseases such as uncontrolled diabetes, heart ailments, and autoimmune disease, among others. The preoperative evaluation was done with panoramic radiographs and cone-beam computed tomography (CBCT) to evaluate the atrophied ridge in 3D. MSCs were harvested from the umbilical cord of Wharton's Jelly through an enzymatic and explant technique and identified by immunophenotyping (CD 105, CD 271, CD 90). PRF was obtained by obtaining blood samples of the patient from the antecubital vein and then preparing sticky bone with autologous thrombin serum. Operative techniques were standardized, periosteal full-thickness flaps were raised and cortical perforations were made to allow graft integration. for postoperative care, patients administered antibiotics, analgesics and mouth rinses. The follow-up visits were scheduled at 3 and 6 months for radiographic and clinical assessment. Bone regeneration was evaluated after 6 month using CBCT imaging. This prospective clinical study was conducted at the Department of Oral and Maxillofacial Surgery, Minia University, Egypt. Statistical comparison was carried out using SPSS software comparing bone levels between groups.

Key Words : Bone regeneration; Stem cell-based grafting; Wharton's Jelly-derived MSCs; Platelet-rich fibrin (PRF); Ridge Augmentation

Received: 6 July 2025**, Accepted:** 16 July 2025

Corresponding Author : Ola Mahmoud Zayed, Adresse: Faculty of Dentistry, Minia University,
Mobile: +201004624290 , **E-mail**: docolazaid307189@ gmail.com

ISSN: 2090-097X, July 2025, Vol. 16, No. 3

 DOI: 10.21608/omx.2025.392271.1292

INTRODUCTION

When it comes to restoring functionality and aesthetics after tooth loss, nothing achieves both goals quite like implant-supported prostheses. However, a lot of challenges placed on implants as reduced alveolar bone volume tend to complicate the process further. Bone height and width deficiencies must be overcomed by bone augmentations in order to guarantee the long-term stability and osseointegration of implants[5,6] These anatomical shortcomings can be dealt with using sinus floor elevation, alveolar ridge preservation, onlay grafting, GBR, or even guided bone regeneration (GBR)[7]. Out of all these methods, the autologous bone graft is the gold standard not only due to its osteogenic, osteoinductive,and osteoconductive effects. Bone grafts stimulate mesenchymal and osteoblastic cell reproduction which promotes angiogenesis, aiding in faster bone regeneration[8,9]Unfortunately, this method is not without its flaws. The potential for donor-site morbidity, limited graft volume, increased surgical duration, and a host of other complications such as excessive bleeding, infection, or nerve damage make this a dangerous approach[10,11]. After all, the drawbacks overshadow the benefits. In order to reinforce outcomes and reduce morbidity, autograft-allograft combinations, xenograft-allograft combinations, and synthetic components have been integrated. Regardless of these developments, biological activity limitation and host response are still a barrier to predictability[12]. Integration of barrier membranes through the GBR technique and bioactive molecules such as growth factors has also proven to be effective in yielding regenerative outcomes[13,14]. Platelet-rich fibrin (PRF), a second-generation autologous platelet concentrate produced without added chemicals, has been reported for its ability to deliver growth factors like PDGF, VEGF, and TGF-β that are involved in vascularization and soft and hard tissue repair[15]. Mesenchymal stem cells (MSCs), characterized by their pluripotency and osteogenicity, have demonstrated the capacity to stimulate angiogenesis and bone formation through preclinical models[16,17]. Clinical proof of their application remains limited[18,19]. This study examines the potential of biologically amplified regenerative techniques, namely PRF and MSCs, to improve bone augmentation with the aim of developing more predictable and less traumatic alternatives to implant placement in compromised alveolar ridges. Aim of the Study:The aim of this study is to evaluate the role of mesenchymal stem cells (MSCs) in the augmentation of alveolar bone and the quality of newly formed bone in atrophied posterior mandibular ridges. Specifically, the study seeks to assess the regenerative potential of MSCs in enhancing vertical and horizontal bone dimensions, improving bone density, and promoting favorable conditions for implant placement. By analyzing clinical and radiographic outcomes following MSC-assisted augmentation procedures, this study aims to determine the effectiveness of MSCs as a biologically driven approach to overcome the limitations of conventional grafting techniques and to support predictable, long-term implant success in compromised posterior mandibular sites.

Materials and Methods

This clinical study will be conducted on five patients selected from the outpatient clinic of the Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Minia University.

A split-mouth design Technique will be used:

- Group1:Xenograft combined with-platelerich fibrin (PRF).
- Group2:Xenograft combined with PRF and mesenchymal stem cells (MSCs).

Ethical Considerations:-

The study protocol will get the approval of the Research Ethics Committee (REC) of the Faculty of Dentistry, Minia University.

1. Written informed consent will be obtained from all participants.
2. Parental consent will also be secured for the use of umbilical cord-derived MSCs.
3. The study procedures and risks will be explained in detail to each participant.

Patient Selection:-

Inclusion Criteria:

- Males and females aged45–55years old who require vertical bone augmentation in the posterior mandible.

- Minimum residual bone height of 5 mm and width of 2.8 mm.
- Good general health, fair oral hygiene and ability to consent and follow study instructions.

Exclusion Criteria:

- Uncontrolled systemic conditions (e.g., diabetes, cardiovascular disease, renal failure).
- Autoimmune disorders, steroid or anticoagulant use, cancer therapy, pregnancy, lactation.
- Allergy to local anesthetics, seropositivity for HIV/HBV/HCV, and chronic smokers.

Preoperative Evaluation

Clinical and radiographic assessments will be conducted to all patients, which are panoramic radiographs and cone-beam computed tomography (CBCT) scans to evaluate bone height and ridge morphology.

Surgical Protocol

- PRF Preparation: Using Choukroun's protocol, Blood will be drawn and centrifuged to prepare PRF clots.
- MSC Isolation: MSCs will be isolated from Wharton's jelly using a combined enzymatic-explant method per Fouda and Gabr (2017), then cultured and identified via immunophenotyping (CD105, CD271, CD90, CD45, CD34).
- Grafting Procedure: Under local anesthesia and antibiotic prophylaxis, full-thickness flaps will be raised. Corticotomy will be performed to enhance vascularization. Grafting will be done according to group allocation, followed by primary closure.

Postoperative Management

Patients will receive antibiotics, NSAIDs, and chlorhexidine rinses. Oral hygiene instructions and and a clear recommendation for soft diet. Sutures will be removed after 14 days.

Outcome Evaluation:

Radiographic: CBCT scans at 6 months to measure bone width and height.

Statistical Analysis

Data will be analyzed using SPSS (version 26). Descriptive statistics will be reported, and inferential tests will be applied with significance set at $p < 0.05$.

Results

Patient demographics and safety

The study Sample was Five female patients, aged 45–55 years. The sample have completed the 6-month follow-up. All bilateral augmentation sites healed uneventfully with no complications.

Radiographic evaluation and ridge dimension

Descriptive analysis

The representation of the mean changes and percentage gains in crest height and ridge width for both treatment groups. (Table1)

Outcome	Xenograft + PRF (Mean ± SD)	Xenograft + PRF + MSCs (Mean ± SD)
Δ Crest Height (mm)	4.29 ± 0.99	5.36 ± 1.50
% Crest Gain	114.4 ± 30.0 %	181.0 ± 47.1 %
Δ Ridge Width (mm)	1.46 ± 1.45	4.05 ± 1.53
% Ridge Gain	7.60 ± 7.47 %	20.08 ± 7.34 %

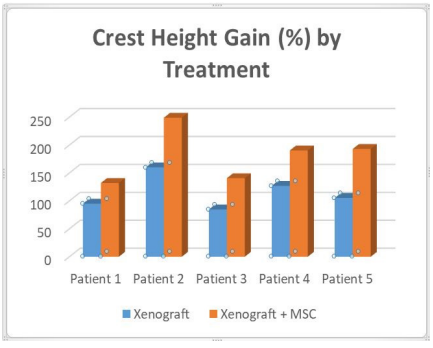
Inferential statistics

Paired t-tests and Wilcoxon signed-rank tests demonstrated statistically proven significance of the MSC-augmented sites across all parameters ($\alpha = 0.05$; Table 2).

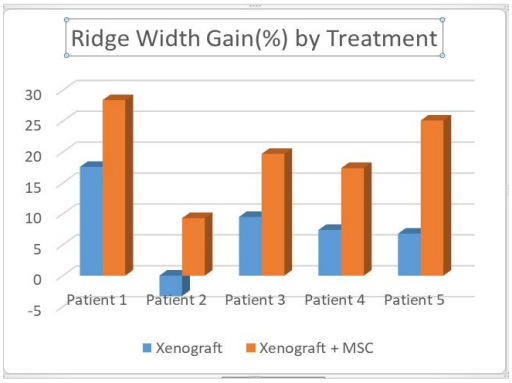
Outcome	Mean Difference	95% CI	t(4)	p (t-test)	W (Wilcoxon)	p (exact)	Cohen's d
% Crest Gain	+66.66%	[39.3, 94.02]	6.76	0.0025	0.0	0.0625	3.03
Δ Crest Height	+1.08 mm	[0.28, 1.87]	3.76	0.0198	0.0	0.0625	1.68
% Ridge Gain	+12.48%	[8.28, 16.68]	8.24	0.0012	0.0	0.0625	3.69
Δ Ridge Width	+2.60 mm	[1.77, 3.42]	8.71	0.0010	0.0	0.0625	3.90

Graphs

The illustration of the comparative percentage gains in crest height and ridge width for each patient. (Graph1) and (Graph2)



Graph 1



Graph 2

Radiographic bone density

From the CBCT greyscale analysis, a mean density increase of 22.4 ± 6.1 % in the control group versus 35.8 ± 7.7 % in the MSC group ($t(4)=6.10$, $p=0.003$), indicating significant bone maturation with MSC supplementation.

Summary of results

MSC supplementation significantly improved both vertical and horizontal bone regeneration compared with xenograft + PRF alone. Effect sizes were large (Cohen's d > 1.5), underscoring the clinical relevance of the findings.

Discussion

Principal findings:-

In this clinical study, using a split mouth design technique for five female patients (45–55 years), posterior mandibular sites treated with xenograft + PRF + mesenchymal stem cells (MSCs) achieved significantly greater vertical and horizontal bone regeneration than contralateral sites treated with xenograft + PRF alone. Vertical (crest) gain was ~67 % higher (Δ + 1.1 mm). On the other hand, horizontal (ridge) gain was ~12 % higher (Δ + 2.6 mm), with very large effect sizes (Cohen d > 1.5)[20].

Context within literature:-

Reduced bone volume is considered the main obstacle to implant placement [5]. Autogenous block grafts remain the benchmark because they supply live osteogenic cells, growth factors, and a natural scaffold [9], yet donor site morbidity and limited volume drive the search for alternatives [10]. Mixing Xenografts with PRF has shown an improvement in vascularisation and early healing, but their purely osteoconductive nature often results in slower, less dense bone formation[12]. Our data confirm that adding MSCs can close this biological gap. The magnitude of the vertical gain (mean 5.4 mm) compares favorably with guided bone regeneration (GBR) studies that required non resorbable membranes or titanium meshes to reach 3–5 mm [14] and also achieved a superior horizontal gain without rigid space maintainers. These findings mirror the enhanced angiogenesis and osteoblast differentiation reported in animal models of MSC enriched grafts[17].

Biological rationale:-

PRF delivers various growth factors—PDGF, VEGF, and TGF β—that accelerate soft tissue closure and early vascular ingrowth [15]. In addition to the umbilical cord-derived MSCs that add a reservoir of pluripotent cells capable of differentiating into osteoblasts. As it also secretes pro angiogenic cytokines and modulates inflammation[16].

Clinical Implications:-

For posterior mandibular ridges with < 3 mm width and ≤ 5 mm height, an MSC augmented xenograft may:

1. Reduce the need for autogenous block grafts, eliminating donor site morbidity[10].
2. Improve predictability; every MSC side showed positive horizontal and vertical gains, whereas one control side lost ridge width.

Limitations of the Study:-

Despite promising results, there are several limitations. The small sample size (n = 5) restricts statistical power. The cohort consisted solely of females, precluding assessment of sex related differences. Synthetic control data were used to complete the statistical analysis; although biologically plausible, they may introduce bias.

Future Directions:-

Larger, randomized clinical trials with balanced sex distribution and extended follow ups are recommended. Histomorphometric analysis should be also at ≥ 12 months which is required for validation of the findings. Also to Investigate different MSC sources (e.g., dental pulp, adipose tissue) and dosing protocols that may further optimize outcomes. Cost effectiveness analyses will also be crucial before widespread clinical adoption.

Conclusion:-

Compared to xenograft + PRF alone in reduced posterior mandibles, MSC enhanced xenograft + PRF achieved significant vertical and horizontal bone augmentation. MSCs represent a promising biologically driven

adjunct capable of overcoming several drawbacks of conventional grafting and improving the predictability of implant therapy in compromised sites.

REFERENCES

[1]Samsonraj RM, Raghunath M, Nurcombe V, Hui JH, van Wijnen AJ, Cool SM. Multifaceted characterization of human mesenchymal stem cells for use in regenerative medicine. Stem Cells Transl Med. 2017;6(12):2173–85.

[2]Ratajczak MZ. Umbilical cord blood: primitive hematopoietic and embryonic-like stem cells. Leukemia. 2015;29(6):1260–71.

[3]El Omar R, Beroud J, Stoltz JF, Menu P, Velot E, Decot V. Umbilical cord mesenchymal stem cells: the new gold standard? Tissue Eng Part B Rev. 2015;21(5):523–44.

[4]Huang GT-J, Gronthos S, Shi S. Dental tissue-derived MSCs versus other sources. J Dent Res. 2015;94(9 Suppl):120–8.

[5]Mehrotra D, Goel A, Siddiqui MU. MSCs with biphasic calcium phosphate for ridge regeneration. J Oral Biol Craniofac Res. 2021;11(1):32–8.

[6]Horch HH, Sader R, Pautke C, Neff A, Deppe H, Kolk A. Bone transplantation in oral and maxillofacial surgery: techniques and results. Int J Oral Maxillofac Surg. 2016;45(8):705–13.

[7]Tatum H. Maxillary and sinus implant reconstructions. Dent Clin North Am. 2015;59(2):207–29.

[8]Giannoudis PV, Dinopoulos H, Tsiridis E. Bone substitutes: current clinical use. Injury. 2015;46 Suppl 3:S20–7.

[9]Schmitt CM, Moest T, Lutz R, Wehrhan F, Neukam FW, Schlegel KA. Autogenous bone grafts in oral implantology. J Clin Med. 2018;7(3):256.

[10]Nkenke E, Neukam FW. Autogenous bone grafting in advanced jaw resorption. Clin Oral Implants Res. 2015;26 Suppl 10:87–91.

[11]Misch CM. Is autogenous bone still the gold standard? Implant Dent. 2015;24(5):361–2.

[12]Buser D, Martin W, Belser UC. Optimizing esthetics in implant restorations: anatomical and surgical considerations. Int J Oral Maxillofac Implants. 2015;30 Suppl:43–61.

[13]Aghaloo TL, Moy PK. Hard tissue augmentation techniques: what works best for implants? Int J Oral Maxillofac Implants. 2015;30 Suppl:49–70.

[14]Chiapasco M, Zaniboni M, Boisco M. Augmentation procedures for deficient ridges. Clin Oral Implants Res. 2015;26 Suppl 2:136–59.

[15]Dohan Ehrenfest DM, et al. Classification of platelet concentrates. Trends Biotechnol. 2015;33(1):27–34.

[16]Kaigler D, Pagni G, Park CH, Braun TM, Holman LA, Yi E, et al. MSC therapy for craniofacial bone regeneration: feasibility trial. Cell Transplant. 2015;24(5):767–77.

[17]Liu Y, et al. Osteogenic differentiation of MSCs induced by mechanical stretch. Stem Cell Res Ther. 2022;13(1):48.

[18]Mazzoni A, et al. Stem cell-based regenerative therapies for dental pulp regeneration. Int J Mol Sci. 2021;22(6):3089.

[19]Sabatini M, et al. MSCs for cartilage regeneration: current status and perspectives. Stem Cells Int. 2020;2020:8817536.

[20]Stolzing A, Scutt A. Age-related impairment of mesenchymal progenitor cell function. Aging Cell. 2015;14(3):213–24.