



Regenerative Dentistry in Pakistan: Awareness, Challenges, and Advancements among General Dental Practitioners and Specialists

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Abstract

Objective Regenerative dentistry has developed a revolutionary advancement in dentistry worldwide. However, significant research still needs to be taken to overcome the challenges in Pakistan. The objective of this study is to evaluate the understanding of general and specialist dentists toward different grafts and their resources during surgical procedures.

Materials and Methods A questionnaire was disseminated for our survey-based study, emailed the soft copy, and distributed the hard copies among 400 general dental practitioners (GDPs) and specialists throughout Pakistan to evaluate the types of grafts used to cover bone or soft tissue defects. Out of 400 GDPs and dental specialists, 200 participants returned the completed questionnaires.

Results Nearly 200 dental surgeons participated from different regions of Pakistan. Most of the GDPs and specialists in Pakistan are not well aware of tissue-engineered grafts and their role in dentistry. The frequency of utilizing a patient's oral fibroblast to generate the collagen is 5.5%. Most of the GDPs are not aware of the resource of bony spicules if utilized which is 49.5%. Consequently, the use of regenerated tissue (oral) grafts is significantly overlooked in Pakistan ($p < 0.001$).

Conclusion Tissue engineering is an extremely encouraging area of reparative biology that attracts the latest innovation in maxillofacial surgery, oral pathology, implantology, cellular and molecular biology, chemistry, and physiology.

Keywords

- ▶ tissue engineering
- ▶ repair
- ▶ regeneration
- ▶ dental grafts
- ▶ cell culture
- ▶ oral lesions

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Introduction

Regenerative dentistry is an evolving arena of medicine involving stem cell technology, tissue engineering, and dental science. It uses biological mechanisms to restore injured oral tissues and their functions.¹ In 2006 an idea was generated by a group of scientists to create a plan for the regeneration of complete human teeth along with all of the supporting structures of dentition.² In the area of modern research, stem cell biology has developed a promising therapeutic strategy, *in vitro* stem cells are used to regenerate several dental soft and hard tissues effectively.³ There is a significant development in the field of stem cell biology to regenerate healthy tissue to replace a defected or diseased tissue. Tissue engineering is an interdisciplinary field that applies the principles of engineering and life sciences to develop biological substitutes to maintain or restore tissue functions.^{4–6} This underpins the regenerative tissue mechanism by isolating healthy cells from the donor (patient). These cells are cultured on suitable scaffold biomaterials, in the form of sheets that act as the template for tissue regeneration to grow a new tissue.⁷

Currently, there is frequent use of autograft during oral and maxillofacial surgery and implantology (tissue sourced from the same organism). Autografts are osteoinductive (undifferentiated cells connect into osteoblast-osteogenesis at sites away from recipient bed) as well as osteoconductive (works as a scaffold in which bone grows from recipient bed).⁸ Allograft (tissue extracted from a different organism of the same species) such as human bone grafts harvested from cadavers in the form of demineralized frozen-dried bone.⁸ Xenografts are tissue harvested from an organism of different species such as pig collagen, rat tail, fish skin, bovine collagen (Bio-Oss), or collagen-derived from coral such as Alipore. These materials are osteoconductive. Although to avoid the risk of immune response and disease transmission the organic component is removed from the graft; however, the risk of infectivity may still be possible.⁸ Alloplastic materials (synthetic grafts) such as hydroxyapatite, tricalcium phosphate, and bioactive glasses are osteoinductive and their approaches are also being developed in dentistry.⁸ Guided bone regeneration/guided tissue regeneration assists to direct the growth of new bone using barrier membranes such as Bio-Gide.⁹ This excludes the ingrowth of fibroblasts and epithelial cells and permits the more slowly growing bone in a protected space. Both resorbable and nonresorbable membranes are available. Membranes must be biocompatible, able to maintain space, and not collapse down and fulfill their primary purpose of cell occlusion to prevent ingrowth of connective tissue cells. At present, platelet-rich fibrin (PRF) has been widely used for regenerative periodontics and wound healing. Regenerative efficacy of the PRF has been assessed for restoring intrabony periodontal defect.¹⁰ The survey aims to analyze the understanding of general dental practitioners (GDPs) and specialist dentists in Pakistan for different types of grafts including engineered tissue grafts. In addition, the use of engineered oral mucosa grafts may develop advancement in dental surgical proce-

dures with better outcomes in terms of healing and tissue architecture.

There are current advancements and progress for the idea of bone restoration by the use of biodegradable materials.¹¹ Tissue engineering is an extremely encouraging area of reparative biology that attracts the latest innovation in maxillofacial surgery, implantology, cellular biology, chemistry, and physiology.¹² Pakistan is a highly populated country and a significant number of people are recorded in the local surgeries and hospitals for the management of oral-maxillofacial trauma, oral cancers, oral premalignant lesions, and dental implant procedures. Unfortunately, there is a limited understanding of tissue engineering in the medical and dental industry in Pakistan. Due to insufficient tissue engineering facilities and deprived collaboration between researchers and clinicians, regenerative dentistry of oral (soft and hard) tissue is not developing momentum in Pakistan. There is a significant need to develop an awareness of using engineered tissue grafts and their resources during surgical procedures among GDPs and specialists in Pakistan.

Materials and Methods

Involvement of the Participants

We drafted a questionnaire for our survey-based study, emailed the soft copy, and distributed the hard copies among 400 GDPs and specialists throughout Pakistan. Each participant was subsequently provided with the questionnaire, consent, and information handouts on the study procedures. The participants were requested to return the completed soft copy of the questionnaire within 3 weeks by email and return the hard copies to the correspondent by post. The participants were nominated randomly from all provinces of Pakistan. Out of 400 GDPs and dental specialists, 200 participants returned the completed questionnaires.

Questionnaire

The questionnaire was designed with demographic details followed by nine multiple choices of questions.^{13,14} The questionnaire was focused on the awareness and priority strategy to use different types of oral graft in different dental procedures. The tool viability and reliability was checked earlier by a pilot study. The following questions were asked:

When do you prefer to place the graft?—During an oral-maxillofacial surgery when there is a loss of more than 1 cm² of tissue due to implant management, managing a tumor/cyst/squamous cell carcinoma, road accident injury: If any other, please specify.

Types of grafts used during the surgical procedures (tick the most appropriate)—Autograft (split-thickness skin, full-thickness graft, and composite graft), allograft (donated cadaveric human skin such as alloderm), xenograft (bovine collagen/bone, fish skin, rat tail collagen), synthetic graft (collagen and bone), or laboratory-generated patient's skin/mucosa/collagen.

What type of collagen is used with or without a bone?—Type I, type II, type III, type IV, or I do not know.

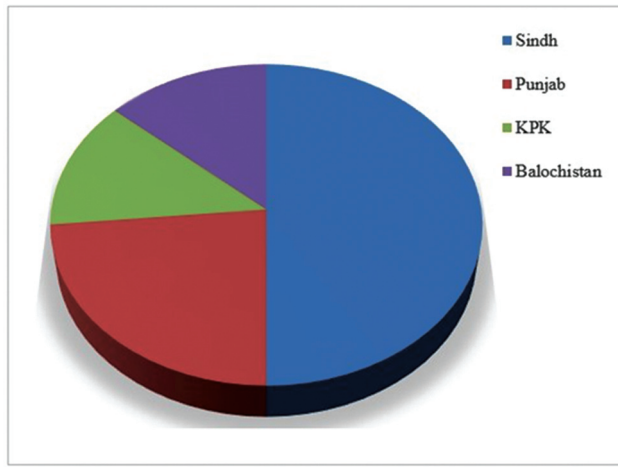


Fig. 1 Demographic distribution analysis of regenerative dentistry in Pakistan.

Do you know the resource of the collagen (membrane) extracted from?—Yes, No, or I do not know.

The bony spicules if utilized are—Laboratory-engineered from the patient bone cells, synthetic, isolated from a cadaver body, or I do not know.

Have you ever used the patient’s oral fibroblasts to generate collagen?—Yes, No, or I do not know.

How often do you use PRF while placing an implant?—Regularly, rarely, or never used.

The quantity of blood most frequently taken to produce PRF in mL/m: 0 to 4 mL, 5 to 9 mL, 10 to 14 mL, or 15 to 20 mL.

Are people well aware of tissue-engineered grafts used during implant placement and oral surgical procedures in the community?—Yes, No, or I do not know.

Results

Demographic Distribution of Dental Surgeon Participation in the Study of Regenerative Dentistry in Pakistan and the Degree of Awareness of Using Engineered Oral Mucosa (Graft) and Their Resources

A total of 200 dental surgeons participated throughout Pakistan, including four provinces, namely, Sindh, Punjab, Baluchistan, and Khyber Pakhtunkhwa (KPK). In Sindh, there were 100 (50%) dental surgeons who participated in the study, while in Punjab there were 47 (23.5%) dental surgeons who were participated in the survey. In Baluchistan, 27 (13.5%) participants were recorded, whereas in KPK there were only 26 (13%) participants registered in the study

(► **Fig. 1**). The *p*-value is calculated as 0.000 or 0.0001 by using the chi-square test, which is less than 0.05 (α) level of significance (► **Table 1**).

Conditions of Using Tissue Grafts

The highest frequency of using graft is during implant management which is 68 (32.7%), oral and maxillofacial surgery which is 56 (26.9%), managing a tumor/cyst/squamous cell carcinoma which is 49 (23.6%), road accident injury which is 23 (11.1%), during periodontal surgery which is recorded as 2 (1%), and the case where it was never used is 2 (1%). The other categories where graft use is reported are periodontal defect, mucogingival defect, infrabony defect, sinus tract augmentation, gingival recession when a bone loss in the maxilla is severe, and close to sinus when the bone loss in the mandible is severe close to the mandibular canal, which have the same frequencies, as 1 (0.5%) (► **Table 2**).

Types of Graft Used during the Surgical Procedure

To analyze the types of grafts used during surgical procedure, we found autograft to be used in 101 (50.5%), synthetic graft in 36 (18%), xenograft in 17 (8.5%), allograft in 15 (7.5%), and laboratory-generated graft in only 3 (1.5%). In contrast, 28 (14%) dentists in our sample did not know about the types of grafts used (► **Table 2**).

Types of Collagen Used with or without Bone

We found the following results when analyzed what kind of collagen is used with or without bone. About 106 (53%) dentists did not know about the types of collagen used during the procedure, while 32 dental surgeons mainly used type II (16%) collagen. Type I is used by 28 (14%) while types III and IV are used by 17 (8.5%) dental surgeons (► **Table 2**).

Understanding the Resources of Collagen

Knowledge about the resource of collagen was reported by 136 (68%) dental surgeons while the understanding has been reported by 64 (32%) dental surgeons. The percentage for the participants who do not know about it is 0% (► **Table 2**).

Frequency of Utilizing Patient’s Oral Fibroblast to Generate the Collagen

To analyze the frequency of utilizing a patient’s oral fibroblast, there is the maximum frequency of “No” reported by 189 (94.5%) dental surgeons and “Yes” by 11 (5.5%) dental surgeons (► **Table 2**).

Table 1 Mean and standard deviation (SD) of awareness value of using engineered grafts and their resources among general dental practitioners

	N	Minimum	Maximum	Mean	SD	<i>p</i> -Value
Frequency of awareness	18	9	206	84.44	61.454	0.0001
Valid N (list-wise)	18					

Table 2 Response of different questions related to the use of different grafts and their resources recorded from the participants

Serial no.	Questions	N	%
1	When do you prefer to place graft?		
	During implant management	68	34.0
	Managing a tumor/cyst/squamous cell carcinoma	49	24.5
	Road accident injury	23	11.5
	During periodontal surgery	1	0.5
	During oral and maxillofacial surgery	50	25.0
	Never used	1	0.5
	Others	8	4.0
2	What types of graft used during surgical procedure?		
	Autograft	101	50.5
	Allograft	15	50.5
	Xenograft	17	50.5
	Synthetic graft	36	50.5
	Laboratory generated	3	50.5
	Don't know	28	50.5
3	What type of collagen used with or without bone?		
	Type I	28	14.0
	Type II	32	16.0
	Type III	17	8.5
	Type IV	17	8.5
	Don't know	106	53.0
4	Do you know about the resources of collagen (membrane) extracted?		
	Yes	64	32.0
	No	136	68.0
5	What are the bony spicules usually used?		
	Laboratory engineered from the patient's bone cells	36	18
	Synthetic	52	26
	Isolated from a cadaver body	12	6
	Don't know	99	49.5
	None	1	0.5
6	The quantity of blood most frequently taken to produce platelet-rich fibrin (PRF)?		
	< 10 mL	35	17.5
	≥ 10 mL	37	18.5
	Don't know	128	64
7	What site of the graft frequently used for reconstruction of bone defect?		
	Maxilla		
	Sinus	68	34
	Buccal/Labial bone	13	6.5
	Sinus lifting	7	3.5
	Labial bone	7	3.5
	Palatal bone	2	1
	Mandible		
	Buccal bone	35	17.5

(Continued)

Table 2 (Continued)

Serial no.	Questions	N	%
	Lingual bone	26	13
	Don't know	42	21
8	Are people aware of tissue engineered graft used during implant placement and oral surgical procedure in the community?		
	Yes	54	27
	No	118	59
	Don't know	28	14
9	Have you ever utilized patient's oral fibroblast to generate the collagen?		
	Yes	11	5.5
	No	189	94.5

Bony Spicules if Utilized

Analyzing the type of bony spicules if utilized, we found that "I don't know" is reported by 99 (49.5%) surgeons, while the frequency of synthetic use is reported by 52 (26%), laboratory engineered from the patient's bone cells is reported by 36 (18%), isolated from a cadaver body is reported by 12 (6%), and none is reported by 1 (0.5%) (→ Table 2).

Frequency of Using Platelet-Rich Fibrin while Placing an Implant

Analyze the frequency of utilizing PRF while placing an implant we have a maximum case as never used by 87 (43.5%), "I don't know" by 80 (40%), rarely used by 15 (7.5%), sometimes and mostly used by 7 (3.5%), regularly used by 2 (1%), and "Yes" and peri-implantitis are recorded by 1 (0.5%) each (→ Table 2).

Quantity of Blood Taken to Produce PRF

To analyze the quantity of blood taken to produce PRF, again the frequency of "I don't know" is maximum as reported by 128 (64%), taken 10 to 14 mL by 31 (15.5%), taken 5 to 9 mL by 30 (15%), taken 15 to 20 mL by 6 (3%), and taken 0 to 4 mL by 5 (2.5%) (→ Table 2).

Awareness about the Tissue-Engineered Graft Used during Implant Placement and Oral Surgical Procedure in the Society

To analyze awareness about the tissue-engineered graft used during implant placement and oral surgical procedure implant and its procedure among people in the society reported by dental practitioners of different provinces was reported as "No" with 118 (59%), "Yes" 54 (27%), and "I don't know" 28 (14%) (→ Table 2).

Discussion

A countrywide pilot study was conducted to update Pakistan's type of graft use strategy. The participation rate in our study was 50%. The response rate was almost similar to other studies using the same methodology.¹⁴ According to the

result of this survey-based investigation, the majority of the participants do not know the type of graft or the graft material they use in their dental practice. This survey revealed that grafts are frequently used during implant management, during the management of tumor/cyst/squamous cell carcinoma, and oral and maxillofacial surgery. According to the survey, mostly autografts are used by dental practitioners. However, most GDPs and specialists are not aware if they implant the ideal type of collagen with or without bone as a graft. Most of the practitioners do not understand the resources of extracted collagen. Interestingly, the study reported that the maximum number of implantologist use bone spicules to enhance healing and repair a bone defect without knowing the resources (such as if bone spicules are synthetic or derived from a cadaver). In addition, the survey evaluated a significant number of dentists who do not know the use of a patient's oral fibroblast to generate a graft. According to the investigation of our study, the frequency of utilizing PRF while placing an implant by practitioners is negligible. It was observed that most of the practitioners take 5 to 10 mL of blood to produce PRF. Our study investigated that more than 60% of dental surgeons in Pakistan are not very well aware of selecting a graft type and engineered oral graft in particular and their resources during surgery and implant procedure. We distributed questionnaires through email and visited them in person as well. We had a few limitations in a study such as we could not include all GDPs and specialists in Pakistan; however, we approached the maximum number of GDPs and specialists. Also, we received incomplete questionnaires from the GDPs and specialists.

Conclusion

There are current advancements and progress for the idea of bone restoration by the use of biodegradable materials. Tissue engineering of oral mucosa could provide a revolutionary therapy in dentistry by generating a graft of the patient's healthy cells. It would bridge a gap between researchers and practitioners to manage premalignant oral lesions, malignant oral lesions, oral ulcerations, burns, and

other oral surgical procedures. This study depicts that there is meager knowledge regarding regenerative dentistry among GDPs and dental specialists in Pakistan. The future study must be conducted for awareness and understanding of regenerative dentistry in Pakistan on a larger scale.

Authors' Contributions

E.K. designed the study. E.K. and N.S. assisted in statistical analysis.

Ethical Approval

The study protocol was approved by the institutional ethical review committee (ESR) Liaquat University of Medical and Health Sciences Jamshoro letter code no: LUMHS/PGMC/-12718.

Funding

None.

Conflict of Interest

None declared.

References

- Miron RJ, Zucchelli G, Pikos MA, et al. Use of platelet-rich fibrin in regenerative dentistry: a systematic review. *Clin Oral Investig* 2017;21(06):1913–1927
- Snead ML. Whole-tooth regeneration: it takes a village of scientists, clinicians, and patients. *J Dent Educ* 2008;72(08):903–911
- Zafar MS, Khurshid Z, Almas K. Oral tissue engineering progress and challenges. *Tissue Eng Regen Med* 2015;12(06):387–397
- Sipe JD. Tissue engineering and reparative medicine. *Ann NY Acad Sci* 2002;961:1–9. Doi: 10.1111/j.1749-6632.2002.tb03040.x
- Aframian DJ, Cukierman E, Nikolovski J, Mooney DJ, Yamada KM, Baum BJ. The growth and morphological behavior of salivary epithelial cells on matrix protein-coated biodegradable substrata. *Tissue Eng* 2000;6(03):209–216
- Alexander H. The clinical impact of tissue engineering. *Tissue Eng* 1995;1(02):197–202
- Kinikoglu B, Damour O, Hasirci V. Tissue engineering of oral mucosa: a shared concept with skin. *J Artif Organs* 2015;18(01):8–19
- Lee RC, Wang Z, Heo M, Ross R, Janssen I, Heymsfield SB. Total-body skeletal muscle mass: development and cross-validation of anthropometric prediction models. *Am J Clin Nutr* 2000;72(03):796–803
- Esposito M, Grusovin MG, Kwan S, Worthington HV, Coulthard P. Interventions for replacing missing teeth: bone augmentation techniques for dental implant treatment. *Cochrane Database Syst Rev* 2008;(03):CD003607
- Najeeb S, Khurshid Z, Agwan MAS, Ansari SA, Zafar MS, Matinlinna JP. Regenerative potential of platelet rich fibrin (PRF) for curing intrabony periodontal defects: a systematic review of clinical studies. *Tissue Eng Regen Med* 2017;14(06):735–742
- Sheikh Z, Najeeb S, Khurshid Z, Verma V, Rashid H, Glogauer M. Biodegradable materials for bone repair and tissue engineering applications. *Materials (Basel)* 2015;8(09):5744–5794
- Pandit N, Malik R, Philips D. Tissue engineering: a new vista in periodontal regeneration. *J Indian Soc Periodontol* 2011;15(04):328–337
- Siaili M, Chatzopoulou D, Gillam DG. Preferences of UK-based dentists when undertaking root coverage and regenerative procedures: a pilot questionnaire study. *Int J Dent* 2014;2014:548519
- Alenzi A, Samran A, Samran A, et al. Restoration strategies of endodontically treated teeth among dental practitioners in Saudi Arabia. A nationwide pilot survey. *Dent J (Basel)* 2018;6(03):44