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A clinic-radiological comparative study to evaluate of hard & soft tissue changes around dental implants placed with platelet rich fibrin in type-2 diabetic patients with varying glycemic levels

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Abstract---Periodontitis is considered the "sixth complication" of diabetes and tooth loss is its inevitable result. Various studies have shown the prevalence of tooth loss to be more in diabetic patients. Poor glycemic levels have shown to affect the osseointegration of dental implants in diabetics, thus this study aimed to evaluate the regenerative and anti-inflammatory effects of Platelet rich Fibrin (PRF) on the peri-implant soft and hard tissue around dental implants in type 2 DM patients with varying glycemic levels. The study was conducted on patients who presented with a complain of missing tooth and required replacement of dentition with endosseous implants at department of periodontis at Rajasthan Dental College & Hospital, Jaipur, Rajasthan. A total of 20 implant sites were selected in 8 patients with age range of 20-65 years. Statistical analysis was carried out using Student t-test' to compare soft tissue evaluation scores and crestal bone loss in both the group. Analysis of variance (ANOVA) was carried out to evaluate the significance between the test and control groups at baseline, 6 and 9 months. On intergroup comparison of bleeding index, probing depth and mesial & distal papilla index between test and control at baseline, loading and 9 months no

statistically significant difference was noted. The only plaque index was statistically significant at baseline, loading and 9 months in between test & control groups. The crestal bone loss in mesial & distal side of implant was statistically significant at baseline, 6 months and 9 months in between test & control groups. We concluded that the usefulness of L-PRF for implant rehabilitation in the diabetic population with varying glycemic levels can only be drawn with longitudinal studies.

Keywords---platelet rich fibrin, endosseous implants, diabetes mellitus, glycemic control.

Introduction

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. Globally, an estimated 422 million adults were living with diabetes in 2014, compared to 108 million in 1980. The global prevalence (age-standardized) of diabetes has nearly doubled since 1980, rising from 4.7% to 8.5% in the adult population.¹ Diabetes caused 1.5 million deaths in 2012. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India.² Raised blood glucose, a common effect of uncontrolled diabetes, may, over time, lead to serious damage to the heart, blood vessels, eyes, kidneys and nerves. Late-onset complications of diabetes can either be microvascular complications or macrovascular complications.

The susceptibility to periodontal disease is the most common oral complication of diabetes.³ Periodontal signs and symptoms are now recognized as the "sixth complication" of diabetes.⁴ Tooth loss is an inevitable result of periodontal disease. Kapp reported that the number of missing teeth was significantly higher in patients with diabetes mellitus.³ Edentulism can lead directly to impairment, functional limitation, physical, psychological, and social disability, and handicap.⁵ Implant therapy is an efficient form of dental rehabilitation that may benefit patients with diabetes mellitus by improving masticatory function and dietary intake, which is critical for diabetic individuals. Dental implant success has been dependent on direct bone-to-implant contact.⁶ Proinflammatory cytokines and growth factors like transforming growth factor, platelet derived growth factor, fibroblast growth factor, epidermal growth factor are released around the implants during healing phase.

There is evidence that hyperglycaemia has a negative influence on bone formation and remodeling and reduces osseointegration of implants. Soft tissue is also affected by the microvascular complications deriving from hyperglycaemia, vascularization of the tissue is compromised, healing is delayed, and wounds are more predisposed to infection.⁶ The microvascularization alteration associated with diabetes leads to a diminished immune response and a reduction in bone remodeling processes. Various studies have substantiated the viability of platelet concentrates on enhancement of osseous and associated tissue healing. PRF is one of the recent innovations of various platelet concentrates. These concentrates

contain high levels of growth factors including PDGF (platelet derived growth factors), transforming growth factors $\beta 1$ and $\beta 2$ (TGF $\beta 1$, $\beta 2$), vascular endothelial growth factors (VEGF), platelet derived endothelial growth factors, Interleukin 1&2, basic fibroblast growth factor (β -FGF), platelet activating factor 4 (PAF-4) .⁷ PRF provides these growth factors at the surgical site to stimulate the healing process.

In dentistry PRF is used for continuity defects, sinus lift augmentation, horizontal and vertical ridge augmentations, ridge preservation grafting, periodontal defects, cyst enucleation, healing of extraction wounds, endodontic surgeries and to treat gingival recession.⁷ Boora et al. evaluated the effect of Platelet PRF on peri-implant tissue response following one-stage implant placement. It was concluded that PRF could be considered as a healing biomaterial with potential beneficial effect on peri-implant tissue and can be used as a therapeutic adjuvant in clinical scenario of one stage. ⁷ As there is sparse evidence about the role of PRF in maintaining the soft tissue integrity and crestal bone alterations in type 2 diabetes mellitus (T2DM) individuals, undergoing implant therapy, the present study is aimed at comparing the soft tissue changes clinically and the crestal bone changes radiographically in type 2 diabetic with varying glycemic levels when dental implants are placed with PRF.

Materials and Methods

The study was conducted on patients who presented with a complain of missing tooth and required replacement of dentition with endosseous implants at department of periodontis at Rajasthan Dental College & Hospital, Jaipur, Rajasthan. A total of 20 implant sites were selected in 8 patients with age range of 20-65 years. Prior to the commencement of implant surgery detailed history of the patients was recorded and were suggested for the following investigations (Preoperative Assessment).

- Test Group: Implants placed with Leucocyte-platelet rich fibrin in type 2 diabetic mellitus patients with HbA1c% - (7.5-8.9%).
- Control Group: Implants placed with Leucocyte-platelet rich fibrin in type 2 diabetic mellitus patients with HbA1c% - (6.5-7.5%).

Inclusion Criteria

- Good oral hygiene and suitability for implant rehabilitation in a 2 stage procedure.
- Sufficient bone volume to receive an implant.
- Edentulous sites in both the arches with D2 type bone.
- Type 2 Diabetes Mellitus with HbA1C levels of 7.5-8.9% ⁸, FBS -167-178 mg/dl, PPBS -189-206 mg/dl ⁹ in experimental group.

Exclusion Criteria

- If any contraindicating factors were present in the planned implant area (eg. Previous tumors, chronic bone disease, previous irradiation).

- If the patient is suffering from any systemic disease other than diabetes mellitus or is on any medication contraindicating implant therapy.
- If the patients is having any parafunctional habits.

Procedure for obtaining leukocyte- and platelet rich fibrin (L-PRF)

L-PRF was prepared according to the protocol developed by Choukroun et al.¹⁰; 10ml of whole venous blood is collected by venepuncture from the antecubital fossa in sterile vacutainer tubes without anti coagulant. The vacutainer tubes are then placed in a centrifugal machine at 3000 rpm for 10 min. The resultant middle layer, containing Platelet Rich Fibrin is segregated. The prepared L- PRF was then compressed using the PRF box to form a membrane and then divided into two parts.

Surgical Procedure

Peri oral preparation with povidine iodine was done followed by rinsing of mouth with 10 ml of 0.2 % chlorhexidine. Surgical area was anesthetized using local anesthesia (2% lignocaine with adrenaline). A mid-crestal incision on the ridge and sulcular incision around the adjacent teeth was placed followed by raising a full thickness mucoperiosteal flap. Soft tissue tags, if any were carefully cleared from the crestal bone with a curette. A crestotome was used to recontour the bone to provide a reasonably flat bed for the implant site whenever needed. Once the implant site is prepared a surgical guide or stent was placed intraorally, and implant site was marked to the depth of 1-2 mm using punch drill or round bur, drilling through the cortical bone. Drill was irrigated copiously with saline internally to prevent over heating of the bone.

Recipient site was verified for position and angulations with paralleling tool. Subsequent drilling was done in sequence to widen the site to accommodate the selected size of implant. The drill speed was reduced from 1200 to 800 rpm as the drill diameter was increased, in order to reduce heating of the bone at the implant site. Once the desired size of the recipient site was achieved, one part of L- PRF was placed into the osteotomy site for the test and the control groups followed by implant placement. Implants were torqued (range) till acceptable level of primary stability was obtained. Cover screw was placed. The implant fixture was then covered with the second part of PRF or the buffy layer – this was followed in both the test and the control group. Flap was then approximated, and suturing was done using simple interrupted sutures with 4/0 silk.

Radiographic evaluation for hard tissue changes

Preoperative radiographic evaluation was done using cone beam computed tomography (CBCT) to assess quality, length and width of the available bone, IOPAR using long cone paralleling technique and OPG. Subsequent evaluation was carried out immediately after loading, 6 months and 9 months after loading using IOPAR with long cone paralleling technique. To standardize radiographic assessment, radiographs were obtained in a constant and reproducible plane using film holder template which was placed in a constant position on the adjacent teeth and an extension arm that could be attached to the film as well as

X-ray tube. Crestal bone levels on both mesial and distal aspects of implants were measured. The apical edge of the implant collar was used as a reference point for the marginal bone level measurements.

Statistical Analysis

Statistical analysis was carried out using Student t-test' to compare soft tissue evaluation scores and crestal bone loss in both the group. Analysis of variance (ANOVA) was carried out to evaluate the significance between the test and control groups at baseline, 6 and 9 months.

Results

A two-stage implant procedure was followed to place all the implants. Over the period of osseointegration (3-4 months for the mandible and 4-5 months for the maxilla), all the implants both in test and control group successfully integrated with the bone without any complications. After the osseointegration period all the implants were restored with screwretained metal-ceramic restorations. No super-structure complication such as chipping, fracture of restorative material or implant complication such as mobility, implant loss and loosening of abutment screw occurred at the follow up visit (6 months and 9 months). On intergroup comparison of bleeding index, probing depth and mesial & distal papilla index between test and control at baseline, loading and 9 months nostatistically significant difference was noted in table no. 1. The only plaque index was statistically significant at baseline, loading and 9 months in between test & control groups. The crestal bone loss in mesial & distal side of implant was statistically significant at baseline, 6 months and 9 months in between test & control groups (Table-2,3).

Discussion

Diabetic patients are considered a relative contraindication for implant therapy due their higher susceptibility to infection, delayed healing, and microvascular complications. Shernoff.et al in 1994 showed a 1 year dental implant success rate of 92.7% for type II diabetic patient under acceptable glucose control.¹¹ Gerardo et al. concluded that in patients with controlled ranges of glycemia implant therapies are predictable.¹² Oates et al .in 2009 showed the decrease in implant stability was significantly greater for subjects with HbA1c of 8.1-10.0% in comparison to subject with HbA1c of 6-8% and non- diabetic subjects.¹³ In 2017, Oates et al conducted a study in poorly controlled diabetic patients in which the survival rates were 98.6% after 1 year and 96.6% after 2 years.¹⁴ The study of Khandelwal treated exclusively patients with poor glycemic control (HbA1c 7.5–11.4 %) and had 98 % implant survival, after 4 months; therefore, he concluded that implant therapy is successful even in poorly controlled diabetes.¹⁵

It is necessary to preserve peri-implant hard and soft tissues for achieving a successful implant therapy. The presence of adequate bone formation and remodeling, a proper immune response and various growth factors enhances the preservation of peri-implant hard and soft tissues, all of which are decreased in a diabetic condition. This can be achieved in diabetic patients by biologically active

molecules, like various growth factors which are expressed during healing and have a positive effect on the healing of both hard and soft tissues. Platelet concentrates are an important source of various growth factors and L-PRF a recent innovation of platelet concentrates can be used in diabetic patients for an improved hard and soft tissue healing around dental implants. A systematic review was conducted by Miron et al.¹⁶ in 2017 to better understand the role of PRF in regenerative procedures.

Majority of studies included in the systematic review have demonstrated favorable results in soft tissue management and repair. The use of PRF helps to achieve the preservation of tooth-like tissue contours and a mature bone tissue around placed implants (Marelli et al., 1958).¹⁷ Plaque is one of the major etiologic factors which may cause tissue destruction around dental implants, thus plaque index score (PI) is one of the diagnostic parameters for monitoring peri-implant conditions. Good plaque control plays an important role in preventing disease around dental implants. In our study, the inter group comparison between the test and controls showed a statistically significant difference. According to the Seventh European Workshop on Periodontology, the clinical parameters that indicate periimplant disease are bleeding on probing (BOP) and increased probing depth. Clinical studies have shown that the key parameter for the diagnosis of periimplant mucositis is bleeding on gentle probing.¹⁸ Our study showed a statistically significant ($P < 0.05$) decline from baseline to 9 month on intra group comparison. However, there was no significance between the test and the control at 9 month follow up, indicating healthy tissues around the implant.

Peri-implant pocket depths presented values that were too low to be considered pathological. Intergroup comparison for probing depth was statistically insignificant. The findings were consistent for 6 and 9 months after loading, insinuating the soft tissue healing capacity of L-PRF in both the groups. Our findings were in comparison to the results attained by Boora et al. (2015)⁹. The microvascular complications in diabetic individuals lead to an deteriorated immune response and bone remodeling. In diabetic subjects, inflammatory processes are increased in chronic hyperglycaemia. There is an elevated level of pro-inflammatory factors, such as tumor necrosis factor (TNF)- α , interleukin (IL)-1b, IL-6 and IL-18. In a study carried out by Abdul Jabbar et al.¹⁹, the inflammatory parameters (PI, BOP and PD) around dental implants was higher in the diabetic group than in the non diabetic patients. The author suggested that the rise in periodontal and periimplant inflammatory response in diabetic patients worsens the inflammatory parameters in such patients. On the contrary, our study presented with no statistical difference on bleeding on probing and periodontal probing depth among the test and control group. The use of L-PRF as an immune node stimulates the defense mechanisms. DingY et al. (2017)²⁰ showed an up-regulation of local growth factor levels, such as PDGF, TGF- β , and VEGF, with resultant blood vessel regeneration resulting in accelerated wound healing on usage of PRF in diabetic mice.

Radiographic evaluation of the peri-implant bone, in addition to assessment of several clinical parameters, has become one of prerequisite for estimating implant success. Grondahl and Lekholm showed a high predictive value of radiographs for the identification of implant stability using the Branemark system. In order to

obtain the most precise readings, computer assisted calibrations were carried out on every implant site measured by evaluating the given distance between several implant threads on the digitized radiograph.²¹ The present study observed that the crestal bone changes on the mesial aspect in the test and control group showed significant difference, while on the distal aspect showed no significant difference. The crestal bone changes on the mesial aspect can be attributed to a variation in oral hygiene maintenance in the region. From a clinical and radiologic point of view at 9 months, the use of PRF as the adjunct for healing seems to be an effective modality to enhance hard and soft tissue healing around dental implants.

Conclusion

The results suggested that the local application of PRF around dental implant has a potential beneficial effect on peri-implant tissue and can be used as a regular protocol in diabetic patients during implant therapy. This study demonstrates a better understanding about the use of autologous platelet rich fibrin in diabetic patients undergoing implant therapy.

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Table 1
Comparison of clinical parameters between test and control group

Follow-Up	Test group			Control group			P value of test vs		
	Baseline	Loading	At 9 months	Baseline	Loading	At 9 months	Baseline	Loading	At 9 months
Bleeding Index	40.68±1.32	38.39±1.04	38.43±0.76	43.64±5.24	41.29±4.33	39.75±4.67	>0.05	>0.05	>0.05
Plaque Index	0.92±0.04	0.73±0.05	0.732±0.06	1.13±0.221	1.03±0.04	0.89±0.03	<0.05	<0.001*	<0.001*
Probing Depth	2.05±0.43	1.84±0.36	1.77±0.32	2.40±0.42	2.16±0.38	2.08±0.38	>0.05	>0.05	>0.05
Mesial Papilla Index	0.76±0.87	0.76±0.87	0.76±0.87	1.11±0.63	0.88±0.84	1.01 ± 0.90	>0.05	>0.05	>0.05
Distal Papilla Index	1.01±0.76	0.88±0.84	0.88±0.84	1.24±0.8	1.36±0.75	1.36±0.75	>0.05	>0.05	>0.05

Table 2
Comparison of crestal bone loss of mesial surfaces in test and control group

	Test	P value	Control	P value	P value of test vs control
Baseline	1.42±0.76		0.67±0.19		<0.05*
6 months	1.53±0.77	>0.05	0.78±0.16	<0.05*	<0.05*
9 months	1.55±0.74	<0.01*	0.82±0.16	<0.05*	<0.05*

Table 3
Comparison of crestal bone loss of distal surfaces in test and control group

	Test	P value	Control	P value	P value of test vs control
Baseline	1.58±1.17		0.71±0.31		>0.05
6 months	1.63±1.18	>0.05	0.77±0.27	>0.05	>0.05
9 months	1.73±1.14	>0.05	0.88±0.29	>0.05	>0.05