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IMMEDIATE VERSUS DELAYED IMPLANT PLACEMENT IN DIABETIC PATIENTS REHABILITATED WITH MANDIBULAR OVERDENTURES – A SPLIT MOUTH STUDY

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ABSTRACT

Purpose: This comparative controlled trial (CCT) evaluates the survival rate of implants placed into fresh extraction sockets and compare it with implants placed in healed sites in type 2 diabetic, completely edentulous subjects rehabilitated with mandibular implant overdentures (MIODs) following a delayed loading protocol and opposed with conventional complete dentures.

Materials and Methods: Fourteen implants were placed in seven well-controlled diabetic subjects as determined by Glycosylated hemoglobin (HbA1c) values before implant placement (baseline) and throughout the follow-up period. Each patient received two implants; one implant in healed canine site and the other was immediately inserted following the extraction of an existing periodontally hopeless canine. The implants were uncovered approximately 3 months after placement and restored with bar-retained overdenture. The patients were scheduled for regular follow-up appointments and for data collection. Kaplan-Meier analysis was used to calculate implant survival from time of prosthesis placement through 24-month follow-up period.

Results: No implant failed in the delayed placement group within the 2 years study period, whereas in the immediate group two implants failed in two patients following the prosthetic loading at one-year follow-up period resulting in 71.2% implant survival rate. HbA1c levels ranging from 7.4 to 8.0 percent were identified in two patients with implant failures. There was no statistically significant difference in survival rate between immediate and delayed implants in type 2 Diabetic subjects rehabilitated with MIOD s (P=0.141).

Conclusions: Within the limitations of this study, insufficient evidence exists to recommend immediate implant placement in type 2 diabetic subjects rehabilitated with MIODs.

KEY WORDS: (Dental implants; Type 2 Diabetes; Immediate placement; Implant survival; Implant overdenture)

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INTRODUCTION

Dental implants proved to be an established treatment modality for the rehabilitation of completely edentulous patients with implant retained and/or supported overdentures. Diabetes mellitus is one of the most common chronic health problems in the world affecting approximately 6% of the population and is considered as a relative contra-indication for implant therapy. However, well-controlled diabetic individuals can have similar success rates for dental implant osseointegration as individuals without diabetes.¹,² The survival rate for implants in diabetic subjects ranges between 88.8% and 97.3% one year after placement, and 85.6% to 94.6% in functional terms one year after the prosthesis insertion. Maintaining adequate blood glucose levels along with the use of pre-operative antibiotics and 0.12% chlorhexidine mouthwash improves the implant survival rate.3 A prospective multicenter study that assessed the success of 2-stage endosseous root-form implants (three different implant systems) placed in the mandibular symphysis of type 2 diabetic subjects restored with an implant-supported, Hader bar clip-retained overdenture found an overall survival rate of over 90% at a 95% confidence interval at 60-month follow-up. The results of the previous study also revealed that the duration of diabetes and length of the implant were significant predictors of implant failures.4

Immediate implant placement at the time of extraction offers several advantages for both practitioners and patients. It allows a reduction in number of surgical procedures, treatment time and consequently an increase in patient satisfaction. Further, immediate implant placement may prevent alveolar bone resorption and thus decrease the need for bone augmentation procedures.⁵ At the Third ITI Consensus Conference,⁶ timing of implant placement was classified based on morphologic, dimensional and histologic changes that follow

tooth extraction. The classifications proposed were type 1 with immediate implant placement in an extraction socket as part of the same procedure, type 2 follows early implant placement typically at 4–8 weeks of healing, type 3 involves early placement at 12–16 weeks of healing, type 4 involves late implant placement at 6 months following extraction. A systematic review ⁷ concluded that the estimated annual failure rate of implants placed in extraction sockets was 0.82% (95% CI: 0.48–1.39%) translating to a 2-year survival rate of 98.4% (97.3–99%).

However, very little is known about the possibility of immediate implant placement in the diabetic patients. To the authors' best knowledge, no previous studies in the literature investigated this topic. Therefore, the aim of the current study was to evaluate the survival rate of type 1, immediately placed implants in diabetic, completely edentulous subjects rehabilitated with mandibular implant overdentures (MIODs) and compare it with type 4, delayed placement in the same patient using a split mouth design.

MATERIALS AND METHODS

Participant selection and study design

The participants were selected from the pool of patients attending outpatient clinic of the Removable Prosthodontic Department, College of Dentistry, MSA University, Egypt. Strict inclusion criteria were as follows: subjects with type 2 diabetes and a mean age of 55.4 years (range 41–68 years), diabetes was well-controlled as assessed by Glycosylated hemoglobin (HbA1c) level in the range of 6.1- 8.0%, subjects were completely edentulous except for unilateral periodontal hopeless mandibular canine indicated for extraction, square arches and a 12 mm or more of vertical clearance was ensured during selection of patients, subjects have worn dentures in both arches for at least 12 months and experienced retention problems with

their mandibular complete dentures, sufficient bone volume and quality in the interforaminal area to receive implants with a minimum of 3.7 mm and 11 mm in diameter and length respectively and no medical contraindications to implant therapy.

Exclusion criteria included smokers and patients with ongoing medications as steroids, anticoagulants, chemotherapy, intravenous bisphosphonates because of potentially impaired healing ability and an increased risk of complications. The patients were given a detailed explanation concerning the present state, alternative treatment plans and the proposed procedures. All patients were informed about the study protocol and objectives before they signed an informed consent. The study was reviewed and approved by Research Ethics committee of MSA University.

Sequence of treatment

Preoperative records

The patients' dentures were duplicated for fabrication of radiographic stent after verifying that the existing denture is well fitted and stable with no rocking, and artificial teeth are in correct position, with correct occlusal plane, and proper vertical dimension (fig.1).

Presurgical implant planning was performed by using CT scan and OnDemand 3D planning software program (OnDemand3D; CD Viewer). Implantation of the missing mandibular canine together with extraction of contralateral periodontally hopeless canine and immediate implant placement was planned (fig. 2 A, B)



Fig. (1) Preoperative Photos. (A) Intraoral photo of maxilla, mandible (B) Patient's old denture. (B) Duplication of patient old denture to be used as radiographic stent, surgical stent

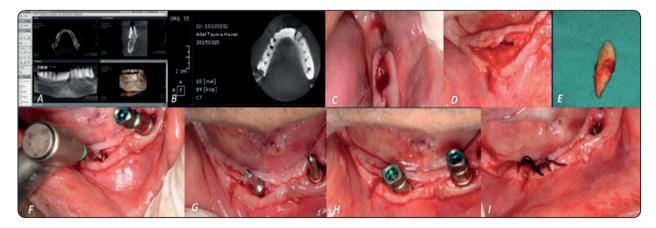


Fig. (2) Preoperative radiographs and Surgical procedure: (A) pre-operative planning using CBCT. (B) pre-operative planning using CBCT. (C) Atraumatic extraction of periodontal hopeless canine. (D) Limited mid crestal incision & Flap (reflection) (E) Extracted canine (F) Drilling (G) Parallel tool placed (H) Implants placement (Delayed implant placement at site 43, Immediate implant placement at site 33) (I) Suturing

Prior to implant placement, diabetes was well controlled by the managing physicians with a regimen of diet alone or diet plus oral hypoglycemic agents and/or insulin as required (Table1). Approximately 14 days before stage I implant placement surgery, the diabetic control of each patient was assessed.

Surgical Procedures

Fourteen implants (Tiologic® Implants, Dentaurum, Ispringen, Germany) were placed in seven patients. Table (1) shows the dimensions of implants that were placed. The implants placed combine cervical chamfer, crestal fine thread and etched/blasted surface that extends to cervical chamfer with modified self-tapping thread geometry. Each patient received two implants; one implant in healed canine site using a limited midcrestal incision (fig 2D) and the other was immediately inserted after extraction of the existing hopeless canine (fig2C,E). All implants were placed by the same operator under local anesthesia (2% lidocaine with 1:100,000 epinephrine) and osteotomies were performed according to the 2-stage protocol suggested by Brånemark,8 A surgical guide was used for every patient to ensure proper angulations and positions of the implants. No bone substitutes or barrier membranes were used for any of immediate implant sites. Excellent primary stability was ensured for both delayed and immediately placed implants. Evaluation of implant stability was made with Osstell mentor device at the day of surgery. The implant stability quotient (ISQ) values were averaged for every implant. Implants showing values ≤65 were not included in the study.

Three weeks postoperatively, the patients' existing mandibular dentures were modified to accommodate the extracted canine, and was then relieved over implant sites and refitted to the mucosa using a tissue conditioner (Visco-gel; Dentsply/DeTrey, Surrey, United Kingdom). Self-monitoring of blood glucose level was performed by patients at the end of the first, second, and fourth week post-

operatively and then monthly until the prostheses insertion. When required, corrective measures for diabetic control were implemented by the managing physician. Stage II implant-uncovering surgery was completed. Three months after implant placement, second stage surgery was performed, implants were exposed and healing abutments were placed.

Prosthodontic Procedures

Fabrication of new complete maxillary dentures and mandibular implant-supported overdentures followed standardized techniques. ⁹

One week following second-stage surgery, the healing collars were removed and impression copings were placed at the implant level (fig.3E). Radiographs verifying precise fit of copings were made. An impression was taken with Impregum polyether impression material (Impregum, ESPE, Seefeld, Germany) at implant level (fig.3F). A cast was then poured and a verification jig was prepared (fig.3H). The verification jig was then checked in the patient's mouth. Splitting and reassembling of non-passive jigs were performed in patients' mouth using duralay (Reliance Dental Mfg Co, Worth,Ill) as shown in (fig.3I).

On mandibular set-up, a silicon index was prepared (fig.3J) to verify the availability of space for the bar attachment (fig.3K). Thereafter, the plastic pattern of bar attachment was mounted on the cast using a surveyor (fig.3L), and the silicon index was replaced on the cast to confirm no interferences with the bar existed (fig.3M). The plastic bar was then tried in patient's mouth (fig.3N). Casting and screwing of metal bar were after accomplished (fig.3O,P). Indirect pick-up of the plastic clip was performed (fig.3Q,R) and dentures were inserted (fig.3S, T). Standardization of laboratory procedures 10 was accomplished with one dental technician using semi- adjustable articulators (bio.art A7Plus Articulator) one type of acrylic resin denture teeth (Vita), and a high-impact denture base acrylic resin (Lucitone, Dentsply). Silicone indices (Elastosil 1470, WackerCheme) were used to record the position of the denture teeth during bar fabrication. Denture teeth were set with lingualized occlusion concept using non anatomic teeth. Laboratory remount and selective grinding procedures were performed, and the occlusion was refined intraorally using articulating paper (Hanel Blue-Red Articulating Paper). Denture base coverage of the supporting mucosa allowed for optimal dentures' support, which was verified on insertion by pressure-indicating paste (Mizzy).

Outcome measure was implant survival. ^{13, 14} The implants were considered surviving if they were clinically stable, functioning without any mobility. Failure was defined as any implant that was removed because of loss of integration, implant

mobility (as verified by Periotest), symptoms as pain, neuropathies, paraesthesia or psychological reason. The estimated failure rate was calculated by dividing the number of events (implant failures) by the total implant exposure time. The total exposure time is the interval of time the implants could be followed for the entire observation time or up to failure of the implants that were lost during the follow-up period.¹⁵

Statistical analysis

Statistical software SPSS (Statistical Package for the Social Science; 22.0, IBM Corp, Armonk, NY, USA) was used in the analysis of the data. Kaplan-Meier analysis was used to calculate implant survival. The mean and median survival

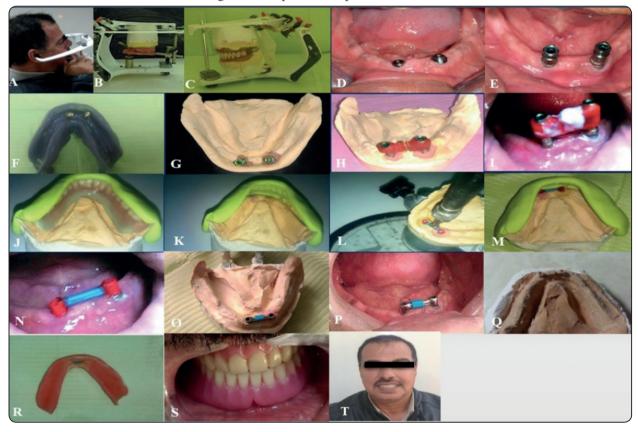


Fig. (3) Prosthetic procedures: (A) Facebow on patient (profile view) (B) Maxillary cast mounted using facebow (C) Set up on semiadjustable articulator (side view) (D) Healing abutment in place (E) Impression coping in place (F) Final impression with analog in place. (G) Trimmed master cast. (H) Splitting of non passive verification jig after check in patient mouth. (I) Reassembling in patient mouth. (J) Index on set up (K) Index after removal of set up. (L) Mounting of bar attachment using surveyor. (M) Index replaced. (N) Try in of plastic bar. (O) Metal bar on cast (P) Cementation of metal bar (Q) Final cast. (R) Pick up. (S) Definitive restoration (Lower bar over denture). (T) Extra oral photo (facial view).

time for each group was calculated with their 95% confidence interval (CI). *P*-values less than 0.05 was considered statistically significant.

RESULTS

After two years, only seven patients could be recruited following the inclusion and exclusion criteria.

Approximately 14 days before stage I implant placement surgery, the mean age of the subjects was 55.4 years (range 41–68 years). The number of years with DM (duration of DM) ranged from 1 to 5 years (mean 2.6). The subjects were controlled with a regimen of diet alone or diet plus oral hypoglycemic agents and/or insulin as shown in table 1. At time of first and second stage surgeries, the HbA1c levels

were within the normal range for the 7 subjects (6.5 to 8.0 %).

No implants failed in the delayed placement group within the 2 years study period, whereas in the immediate group two implants failed in two patients at one-year follow-up period resulting in 85.7% overall implant survival rate for the 2 groups. HbA1c levels ranging from 7.4 to 8.0 % were identified in two patients with implant failures. Both patients were on diet regimen plus insulin for the management of diabetes.

There was no statistically significant difference in survival rate between immediate (71.4%) and delayed (100%) implant placement in type 2 diabetic patients restored with MIODs (P=0.141). The survival rate of implants is shown in Kaplan-Meier graph as presented in fig 5 and table 2.

TABLE (1) Implant failure and survival period, dimensions of inserted implants, duration of diabetes and patient medication

	Implant failure	Survival	Dimensions of	Medications	Duration of
	Y/N	Period(M)	implants (L/D)		diabetes(Y)
Immediate implant 1	Yes	11m	11/3.7	Regimen of diet plus insulin	3Y
Immediate implant 2	No	24 m	11/3.7	Regimen of diet plus insulin	5Y
Immediate implant 3	Yes	12m	13/3.7	Regimen of diet plus oral hypoglycemic agents and Insulin	2 Y
Immediate implant 4	No	24 m	13/3.7	Regimen of diet plus insulin	2Y
Immediate implant 5	No	24 m	11/3.7	Regimen of diet plus oral hypoglycemic agents	1Y
Immediate implant 6	No	24 m	11/4.2	Regimen of diet plus Insulin	2Y
Immediate implant 7	No	24 m	11/3.7	Regimen of diet plus oral hypoglycemic agents	3Y
Delayed implant 1	No	24m	11/3.7	Regimen of diet plus Insulin	3Y
Delayed implant 2	No	24 m	13/3.7	Regimen of diet plus Insulin	5Y
Delayed implant 3	No	24m	11/4.2	Regimen of diet plus oral hypoglycemic agents and Insulin	2Y
Delayed implant 4	No	24 m	11/3.7	Regimen of diet plus Insulin	2Y
Delayed implant 5	No	24 m	13/3.7	Regimen of diet plus oral hypoglycemic agents	1Y
Delayed implant 6	No	24 m	13/3.7	Regimen of diet plus Insulin	2Y
Delayed implant 7	No	24 m	11/3.7	Regimen of diet plus oral hypoglycemic agents	3Y

TABLE (2) Kaplan-Meier analysis for survival rates in both groups

Kaplan-Meier

Case Processing Summary

			Censored	
Group	Total N	N of Events	N	Percent
Immediate	7	2	5	%71.4
Delayed	7	0	7	%100.0
Overall	14	2	12	%85.7

Survival Table

Group		Time	Status	Cumulative		N of Cumulative	N of Remaining
				Survival rate	Std. Error	Events	Cases
Immediate	1	11.000	1	0.857	0.132	1	6
	2	12.000	1	0.714	0.171	2	5
	3	24.000	0	•		2	4
	4	24.000	0	•		2	3
	5	24.000	0			2	2
	6	24.000	0	•		2	1
	7	24.000	0			2	0

Overall Comparisons

	Chi-Square	df	p value
(Log Rank (Mantel-Cox	2.163	1	0.141

Test of equality of survival distributions for the different levels

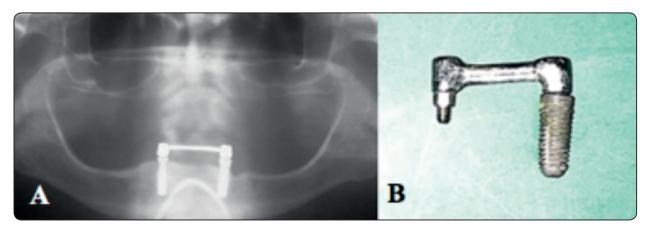


Fig. (4) Immediate implant failure A-Panoramic view showing failed immediate implant B-Failed immediate implant removed with bar super-structure

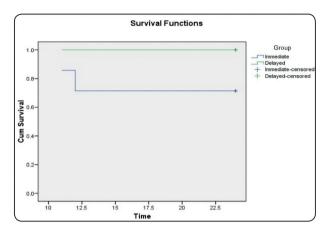


Fig. (5) Survival curve for immediate, delayed implant groups

DISCUSSION

This controlled clinical trial evaluated the survival rate of type 1, immediately placed implants in diabetic, edentulous subjects rehabilitated with mandibular implant overdentures (MIODs) and compared it with type 4, delayed placement in the same patient using a split mouth design. Fourteen implants were placed in 7 patients; 7 implants were immediately placed in the extraction socket and 7 implants were placed in a fully healed socket 6 months following extraction. No failures occurred in delayed placement group while 2 implants failed in the immediate group resulting in an overall survival rate of 85.7 %. Both failures occurred after one year of functional loading, which is in congruence with data reported from previously published studies. The fact that most failures occur after the secondphase surgery and during the first year of functional loading may be related to mechanical characteristics of the newly formed bone in form of a reduced percentage of bone-to-implant contact, immature bone, or incorrectly formed bone. 16,17,18 Following the functional loading of the implants, mechanical overload of the bone with reduced mechanical properties may occur and result in the observed failures. 16 Further, the long-term maintenance of the osseointegration is dependent on physiologic bone remodeling. A number of studies revealed that bone and mineral metabolism are altered in diabetes.

Diabetes decreases the rate of bone formation and alters remodelling, which may be best explained by collagen abnormalities in response to advanced glycosylation end products (AGE) detected in diabetic cases.¹⁹

An overall implant survival rate of 85.7% and 100% for delayed implant placement group is in agreement with previous literature that reported survival rate for implants in well-controlled diabetic subjects that ranges between 85.6% to 94.6% one year after the prosthesis insertion. Strict glycemic control can reduce micro-vascular complications of diabetes and help improve the function of osteoblast, and result in successful dental implant osseointegration and high implant survival rates.²⁰

The 71.4% implant survival rate, which is observed for immediate implant placement, is lower than that reported for the general population without diabetes, which is in the range of 94 to 100 % over healing period of 3 months to 7 years. In all immediate implant sites, no bone substitutes or barrier membranes were used, even if there were gaps between the implant and the bone of the extraction socket. It was demonstrated that when using the submerged technique with a gap between the implant and the bone, there is a strong tendency for the defect to fill in with bone in both the horizontal and the vertical planes in various degrees depending on gap size without the use of barrier membranes and bone substitutes. 21,22 Immediate functional loading of immediate implants without the use of any bone substitutes or barrier membranes for fixed complete-arch reconstructions can be successful over a 2-year period.²³ The altered bone and mineral metabolism in case of diabetes, with decreased osteoblast differentiation and proliferation and decreased collagen production may have interfered with the bone fill of the defect. The later described combined with the lack of use of any bone substitutes may be the reason of failures observed in immediate placement group in the present study. For future research, it would be of interest to evaluate the influence of placing barrier membrane and bone substitutes on the survival rate of immediately placed implants in diabetic patients and whether this will have an influence or not on the long-term prognosis of treatment. Accordingly, recommendations can be formulated regarding the clinical protocol to maximize the restoration of diabetic patients with dental implants.

Based on the findings of this study, it can be concluded that insufficient evidence exists to recommend immediate implant placement in diabetic patients. Lack of statistical significance in survival rate between the two groups may be related to small sample size rather than the difference in treatment protocol between the two groups. However, because of the strict inclusion criteria including non-smokers, diabetic and completely edentulous patients except for a hopeless lower canine only seven patients could be recruited throughout the whole study period. Non- smokers were selected for this study because the deleterious effect of smoking on osseointegration.²⁴ The combination of smoking and diabetes may substantially increase the risks of implant failure. Therefore, for the design of future prospective studies, multicenter studies are recommended to enable the recruitment of maximum number of participants and the drawing of solid, evidence-based recommendations. Further, sample size calculation was not possible at the offset of the study due to the lack of any studies in the literature that evaluated survival rate of immediately placed implants in diabetic patients. Despite the limitations mentioned, this study represents an initial step to delve deeper into clinical protocol that should be implemented to maximize the treatment outcome of dental implants in diabetic subjects.

CONCLUSIONS

Insufficient evidence exists to recommend immediate implant placement in type 2 diabetic subjects rehabilitated with MIODs. Well-designed prospective clinical studies are recommended to optimize implant treatment of diabetic subjects and formulate evidence-based clinical protocol.

Authorship

This research has been read and approved by all authors and all authors agree to the submission of the manuscript.

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Conflict of interests

The authors declare that they have no conflict of interests.

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REFERENCES

- Morris HF, Ochi S, Winkler S. Implant Survival in Patients with Type 2 Diabetes: Placement to 36 Months. Annals of Periodontology. 2000, 5: 157-165.
- De Araújo Nober M, Malo P, Gonçalves Y, Sabas A.
 Dental implants in diabetic patients: retrospective cohort study reporting on implant survival and risk indicators for excessive marginal bone loss at 5 years. J Oral Rehab. 2016; 43: 863-870.
- Mellado-Valero A, Ferrer- García J-C, Herrera-Ballester A, Labaig-Rueda C. Effects of diabetes on the osseointegration of dental implants. Med. oral patol. oral cir. bucal.2007; 12: 38-43.
- Olson JW, Shernoff AF, Tarlow JL, Colwell JA, Scheetz JP, Bingham SF. Dental endoseeous implant assessments in a type 2 diabetic population: A prospective study. Int J Oral & Maxillofac Implants. 2000;15: 811-818.
- Tonetti MS, Cortellini P, Graziani F, Cairo F, Lang NP, Abundo R, Conforti GP, Marquardt S, Rasperini G, Silvestri M, Wallkamm B, Wetzel A. Immediate versus delayed implant placement after anterior single tooth extraction: the timing randomised controlled clinical trial. J Clin Periodontol. 2017; 44: 215-224.

- Hämmerle, C.H., Chen, S.T. & Wilson, T.G., Jr. Consensus statements and recommended clinical procedures regarding the placement of implants in extraction sockets. The International Journal of Oral Maxillofacial Implants. 2004; 19: 26–28.
- Lang, N. P., Pun, L., Lau, K. Y., Li, K. Y. &Wong, M. C. M. A systematic review on survival and success rates of implants placed immediately into fresh extraction sockets after at least 1 year. Clin Oral Implants Res 2012; 23: 39–66.
- Lekholm U, Zarb G. Patient selection and preparation.
 In: Branemark PI, Zarb G, Albrektsson T, eds.: Tissue integrated prosthesis: osseointegration in clinical dentistry.
 Chicago. Quintessence Publishing Co Inc. 1985:199-209.
- Mericske-Stern R, Zarb GA. Clinical protocol for treatment with implant-supported overdentures. In: Zarb GA, Bolender CL, Carlsson GE (eds). Boucher's Prosthodontic Treatment for Edentulous Patients, ed 11. St Louis: Mosby. 1997:518–530.
- Beumer J, Lewis S. The Brånemark Implant System: Clinical and Laboratory Procedures. St Louis: Ishiyaku; 1989.
- 11. Lang BR, Razzoog ME. Lingualized integration: Tooth moulds and an occlusal scheme for edentulous implant patients. Implant Dent.1992;1:204–211.
- Wismeijer D, van Waas MAJ, Kalk W. Factors to consider in selecting an occlusal concept for patients with implants in the edentulous mandible. J Prosthet Dent. 1995; 74:380– 384.
- Albrektsson, T, Zarb, GA. Current interpretations of the osseointegrated response: clinical significance. Int J Prosthodont. 1993; 6:95–105.
- 14. Ross J, Sennerby L, Lekholm U, Jemt T, Gröndahl k, Albrektsson T. A qualitative and quantitative methods for evaluating Implant success: a 5-year retrospective analysis of Branemark implant. Int J Oral & Maxilofac Implants. 1997; 12: 504-514.

- Pjetursson, B. E., Tan, W. C., Zwahlen, M. & Lang, N. P. A systematic review of the success of sinus floor elevation and survival of implants inserted in combination with sinus floor elevation. Journal of Clinical Periodontology. 2008; 35, 216–240.
- Fiorellini JP, Chen PK, Nevins M, Nevins ML. Retrospective study of dental implants in diabetic patients. Int J Periodontics Restorative Dent. 2000; 20:367-373.
- 17. Farzad P, Andersson L, Nyberg J. Dental implant treatment in diabetic patients. Implant Dent 2002; 11:262-267.
- Peled M, Ardekian L, Tagger-Green N, Gutmacher Z, Matchei EF. Dental implants in patients with type 2 diabetes mellitus: a clinical study. Implant Dent 2003; 12:116-138.
- Monnier V.M., Sell D.R., Genuth S. Glycation products as markers and predictors of the progression of diabetic complications. Ann. NY Acad. Sci. 2005; 1043:567–581
- Javed F., and Romanos GE. Impact of diabetes Mellitus and glycemic control on the osseointegration of dental implants: A systematic literature review. J Periodontol 2009; 80: 1719-1730.
- Nir-Hadar O, Palmer M, Soskolne WA. Delayed immediate implants: Alveolar bone changes during the healing period. Clin Oral Implants Res. 1998;9: 26–33.
- Akimoto K, Becker W, Persson R, Baker DA, Rohrer MD, O'Neal RB. Evaluation of titanium implants placed into simulated extraction sockets: A study in dogs. Int J Oral Maxillofac Implants. 1999;14: 351–360.
- Grunder u. Immediate Functional Loading of Immediate Implants in Edentulous Arches: Two-Year Results. Int J Periodontics Restorative Dent. 2001; 21:545–551.
- Vervaeke S, Collaert B, Cosyn J, Deschepper E, De Bruyn H. A multifactorial analysis to identify predictors of implant failure and peri-implant bone loss. Clin Implant Dent Relat Res. 2013; 17:298–307.