

Vol. 64, 635:644, January, 2018

I.S.S.N 0070-9484



FIXED PROSTHODONTICS, DENTAL MATERIALS, CONSERVATIVE DENTISTRY AND ENDODONTICS

www.eda-egypt.org

Codex: 192/1801

EFFECT OF GLYCEMIC CONTROL ON IMPLANTS ASSISTED MANDIBULAR OVERDENTURES

Ahmed M. Alam-Eldein*, Tamer M. Nasr Mostafa* and Emad A. Mabrouk*

ABSTRACT

Purpose: This study was conducted to evaluate the effect of glycemic control on implants assisted mandibular overdentures in type II diabetic patients after three years of function. **Materials and Methods:** Thirty, completely edentulous patients with a mean age of fifty years old were included in this study. For each patient two implants (3.5*13mm Anyone Two— piece dental implant, Mega Gen Implant System, Korea) were placed at the canine region bilaterally with equator attachment to retain mandibular overdenture. Patients were distributed into two groups: Group (1) contained patients who their glycemic control values below 8%. Group (2) contained patients who their glycemic control values 8% or above 8%. Each patient was evaluated clinically concerning plaque index, probing depth and implant stability by using resonance frequency analysis and radiographically concerning marginal bone loss at baseline (overdenture insertion) and after 6, 12, 24, 36 months after insertion. Data were collected, tabulated and statistically analyzed using t-Student test.

Results: There was a statistically significant difference between both groups (P < 0.05) regarding probing depth, implant stability and marginal bone loss

Conclusions: Wither the limitations of this short term study, glycemic control seems to have an effect on the survival of implants assisted complete overdentures in type II diabetic patients.

KEYWORDS: Dental implant, Glycemic control, Implant overdenture, Type II diabetes.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder that is reaching epidemic proportions ¹. It is a common metabolic disorder characterized by hyperglycemia due to impaired insulin secretion, insufficient insulin action, or both. The main types of diabetes include type 1 and type 2 diabetes. Type 1 diabetes is associated with pancreatic b-cell

destruction and accounts for 5% to 10% of the subjects with diabetes. Type 2 diabetes is associated with a relative, rather than an absolute, insulin deficiency and accounts for 90% to 95% of all individuals with diabetes ².

Diabetes mellitus has long been considered a relative contraindication to dental implant therapy. Our understanding of diabetes mellitus as

^{*} Lecturer, Prosthodontic Department, Faculty of Dentistry, Tanta University,

a relative contraindication, based on the patient's level of glycemic control, has changed little since the 1988 NIH Consensus Conference on Dental Implants ^{3, 4}. This appears appropriate given the correlations between glycemic control and micro and macro-vascular complications. As a result, well-controlled diabetic patients may be considered appropriate for implant therapy while diabetic patients lacking good glycemic control may be denied the benefits of implant therapy ⁵.

Glycated hemoglobin (HbA1c) is becoming the most frequently used and valuable diagnostic and therapeutic measure of blood glucose control. This value represents the percent of glycated hemoglobin in red blood cells. Because this value is based upon the average circulating time of a red blood cell, 60–90 days, it reflects longer term or average blood glucose levels over two to three months. Elevated HbA1c levels correlate directly with morbidity and mortality in diabetes ⁶. Therefore, achieving low HbA1c levels serves as an important therapeutic target in the management of diabetes ⁷. Recent recommendations for strict glycemic control for persons with diabetes have targeted maximal HbA1c levels ranging from 6.5% up to 7.0% ⁸.

A prospective study evaluated implant survival after one year of restoration in patients with HbA1c levels between 8.1% and 10.0% reported no implant failures suggesting that short-term loading of the implants may not be detrimental to implant success in this patient population ⁹.

A systematic review examined the evidence available for the use of implant therapy for patients with diabetes based on glycemic control and the potential for glycemic control to serve as an appropriate discriminator for the application of care reviewing clinical studies; no clinical data were found supporting a significantly increased risk of implant failure for patients lacking good glycemic control ¹⁰.

The effect of glycemic level on implant integration in persons with diabetes remains poorly

understood, while support is emerging for implant therapy in diabetic patients with appropriate accommodations for delays in implant integration based on glycemic control. The aim of this study was to evaluate the effect of glycemic control on implants assisted mandibular overdentures in diabetic patients after three years of loading.

MATERIALS AND METHODS

This study was carried out on thirty completely edentulous, Type II diabetic patients with a mean age of 53 years old. Patient's general health was evaluated by taking a full medical history. Laboratory investigations included the Glycosylated Hemoglobin Test (HbA1c Test) were performed to distribute the patients over the two study groups, all patients with HbA1c levels below 8% were included in group I, while patients whose HbA1c level were 8% or above 8% were included in group II.

Cone Beam CT were taken for all patients to show the height and width of bone as well as the bone density in the interforaminal area, the position of the mental foramen and inferior alveolar canal and to check for any clinically undetectable pathology or bone abnormality. An informed consent approved by the ethics committee was signed by each patient after discussing the treatment plan with them and prior to initiation of treatment.

An acrylic complete denture was fabricated for each patient with the conventional technique using semi-anatomic acrylic teeth set on semi-adjustable articulator. These acrylic dentures were duplicated using clear autopolymerized acrylic resin to produce surgical templates to aid in implant insertion in the proper canine regions. For each patient, two mandibular immediately-loaded (3.5*13mm Anyone Two- piece dental implant, Mega Gen Implant System, Korea) were placed using flapless technique, with equator attachments to retain mandibular overdentures. (Fig. 1& 2).

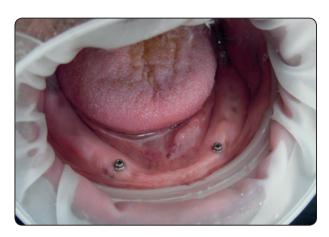


Fig. (1): The two implants with equator attachments inserted in the mandibular edentulous arch.

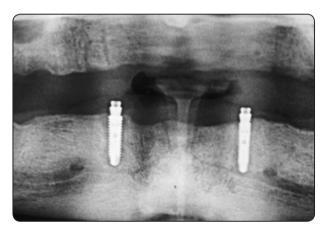


Fig. (2): A radiograph of the two implants with equator attachments inserted in the mandibular edentulous arch.

Twenty four hours after implant insertion; patients were recalled and each mandibular denture was relieved at the implant locations, the plastic caps were placed on the implants making sure that the dentures were securely seated, the head of each implant was then covered with a small shim to prevent excess acrylic resin from engaging any undercuts. The relieved areas of the fitting surface of the denture were filled with autopolymerized acrylic resin, dentures were seated and patients were instructed to bite gently during setting of the acrylic resin. After the resin set, the dentures were removed, the plastic caps inside the dentures were examined, any excess resin was trimmed and inserted in the patient's mouth. Patients were then

instructed on how to clean the denture and were asked to return on the following day to examine the denture bearing area and check for signs of tissue irritation. All patients were then scheduled for clinical and radiographic follow-up visits.

For group I: Each patient was asked to deliver the Glycosylated Hemoglobin Test (HbA1c Test) every three months all over the study period to ensure glycemic control with Glycosylated Hemoglobin levels were below 8.0%.

For group II: Each patient was asked to deliver the Glycosylated Hemoglobin Test (HbA1c Test) every three months all over the study period to ensure glycemic control with Glycosylated Hemoglobin levels were 8% or above 8%.

For patients of group II which demonstrated Glycosylated Hemoglobin levels below 8.0% were shifted to group 1 and vice versa.

Patients were evaluated clinically and radiographically at baseline (complete denture insertion) and at 6, 12, 24 and 36 months after complete denture insertion as follows:

Plaque index:

Plaque adherent to implants' surfaces was quantified at four sites, buccal, lingual, mesial and distal, using a mouth mirror and a plastic dental explorer after air drying of the implant and gingiva. Each of the four areas was scored on a 4-point scale of 0-3 as described by Mombelli and Lang ¹¹:

- 0 = No plaque is visible
- 1 = A film of plaque adhering to the free gingival margin and adjacent area of the implant, seen only after application of disclosing solution or by running the explorer across the implant surfaces.
- 2 = Moderate accumulation of soft deposits within the gingival pocket and on the gingival margin and/or adjacent to implant surface that can be seen by the naked eye.

3 = Abundance of soft matter within the gingival pocket and/or the gingival margin and adjacent implant surface.

The PI score was obtained by taking the average of the four plaque scores for the single implant.

Probing depth 12:

The probing depth was measured using a plastic periodontal probe (CPITN, R.O.R. international, Copenhagen, Denmark) around the surfaces of the implants in four areas (mid-buccal, mid-lingual, mid-mesial and mid-distal). The score was obtained by taking the average of the four scores for the single implant and. Measurements of probing depth ≤1 mm was recorded as 1mm, measurements exceeding 1mm, but less than 2 mm was recorded as 2 mm, and so on.

Stability test by using OSSTELL ISQ (Implant stability quitent) (Osstell Mentor Göteborg, Sweden) ¹³:

- > Smart peg was inserted inside the fixture and firmly screwed into it.
- ➤ The probe of Osstell was directed toward the smart peg without touching it (3mm away from it) in two directions bucco- lingual and mesiodistal.
- > The average of two readings was calculated.
- ➤ Values less than 50 ISQ have a higher risk of failure. An increase in ISQ value during long-term examination implies that the implant became more stable ¹⁴. Reports indicate that ISQ values are proportional to the extent of bone formation ¹⁵.
- ➤ Reading above 50 ISQ indicate stable implants.

Periapical and Panoramic radiographs 16:

Periapical and Panoramic X-ray films were used to measure the marginal bone loss around the implants. The long cone paralleling technique using the

Rinn XCP instrument (Rinn Co. Dentsply division, York, PA, USA) was used. It included the use of standardized periapical radiographs to detect changes in alveolar bone surrounding the implants during the follow-up period. The standardized periapical radiographs were taken by the Xerograph Coping Process holder with a personalized bite registration record, made from putty rubber base impression material for extension cone (35 cm) paralleling technique. Every X-ray film was inserted into a slot in the bite-block. To ensure accurate repositioning of the film every time the radiograph was taken, the putty rubber base impression material (Express XT VPS, 3M ESPE AG, Germany) was folded around the bite-block, then a bite registration was obtained for each film in closed mouth position, the putty bite-block with the occlusal registration was kept aside for the follow-up recall visits. Repeatable standardized periapical radiographs were made for each implant to measure the mesial and distal bone heights. The measurements were made from the base of the implant to the most coronal point of bone adjacent to the implant surface.

All radiographs were exposed using ultra speed periapical film (Kodak, Paris, France) with X-ray grid and X- ray unit set at 70 KV and 10 mA. With similar exposure times, the radiographs were developed under standardized condition using automatic process. The scanning settings were adjusted and noted down in order to be used each time with all the radiographs before each scan, 2600 DPI (dot per inch) high quality resolution, 100% (1:1) scaling, fixed brightness and contrast setting, and no filter or other modifications were selected. The images were displayed on a 17 inches View sonic (3) colored monitor (1024 x 768 DPI). The digital image was then saved in an uncompressed format on the patient file. The stored images of each patient were then interpreted at the end of the follow-up period.

The marginal bone-level measurements were made from the reference point to the lowest observed point of contact of the marginal bone with the fixture. The reference point for the fixture was the fixture—abutment interface. The distance was measured to the nearest 0.01 mm. These measurements were done using an analysis software program (Adobe Photoshop, Adobe Systems Incorporated, San Jose, CA, USA). The actual implant length served as a standard to calculate the bone height, calculations were made according to the following formula:

CBL = IL*BR/MIL

Where **CBL** is the calculated bone resorption, **IL**: Actual implant length, **BR**: measured bone resorption (mean mesial and distal) and **MIL**: measured implant length.

Data analysis:

All clinical and radiographic data were tabulated for each individual and group. Summary statistics (mean, standard deviation) were calculated and also tabulated; data were statistically analyzed using t-Student test.

RESULTS

Plaque Index:

On the initial examination after prosthesis insertion, mean \pm standard deviation (SD) of plaque index scores of group I patients was (3.89 \pm 0.44), while mean \pm standard deviation (SD) of plaque index scores of group II patients was (3.96 \pm 0.51). During the follow-up period there was a nonsignificant statistical decrease of the plaque index (P 0.05 >) between the two groups.

Probing Depth:

On the initial examination after prosthesis insertion, mean±standard deviation (SD) of probing depth scores of group I and group II patients was (1 ± 0) . After 6 months, there was a non-significant statistical increase of the probing depth (P 0.05 >) between the two groups. While after 12, 24, 36 months there was a significant statistical increase of the probing depth between the two groups (P < 0.05)

TABLE (1) Comparison of plaque index at different follow up periods.

DI I J	Group I	Group II	T-test	
Plaque Index	Mean ± SD	Mean ± SD	t	P-value
Insertion	3.89 ± 0.44	3.96 ± 0.51	1.54	0.546
After 6 Months	3.47 ± 0.52	3.61 ± 0.57	1.66	0.437
After 12 Months	3.15 ± 0.38	3.27 ± 0.44	1.39	0.624
After 24 Months	3.02 ± 0.32	3.14 ± 0.37	1.44	0.379
After 36 Months	2.79 ± 0.28	2.99 ± 0.29	1.47	0.446

TABLE (2) Comparison of probing depth at different follow up periods.

Probing Depth	Group I	Group II	T-test	
	Mean ± SD	Mean ± SD	t	P-value
Insertion	1 ± 0	1 ± 0	0	1
After 6 Months	1.25 ± 0.54	1.31 ± 0.63	1.67	0.429
After 12 Months	1.33 ± 0.62	1.49 ± 0.76	1.35	0.03*
After 24 Months	1.49 ± 0.57	1.67 ± 0.69	1.73	0.01*
After 36 Months	1.55 ± 0.68	1.89 ± 0.72	1.55	0.001*

^{*}Significance: P < 0.05

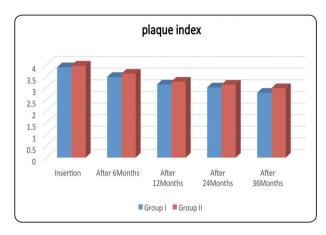


Fig. (3): Distribution of mean value of plaque index between the two groups at different follow up periods.

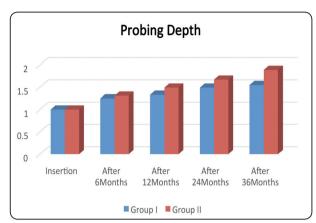


Fig. (4): Distribution of mean value of probing depth between the two groups at different follow up periods.

Stability Test (Osstell ISQ):

On the initial examination after prosthesis insertion, mean \pm standard deviation (SD) of stability test scores (Osstell ISQ) of group I patients was (52.463 \pm 3.537), while mean \pm standard deviation (SD) of stability test scores (Osstell ISQ) of group II patients was (51.835 \pm 3.246). After 6 months, there was a non-significant statistical increase of the stability test scores (Osstell ISQ) (P0.05>) between the two groups. While after 12, 24, 36 months there was a significant statistical increase of the stability test scores (Osstell ISQ) between the two groups (P < 0.05)

Marginal bone loss:

On the initial examination after prosthesis insertion, mean \pm standard deviation (SD) of marginal bone loss scores of group I patients was (0.95 \pm 0.45), while mean \pm standard deviation (SD) of marginal bone loss scores of group II patients was (0.98 \pm 0.65). After 6 months, there was a nonsignificant statistical increase of the marginal bone loss (P 0.05 >) between the two groups. While after 12, 24, 36 months there was a significant statistical increase of the marginal bone loss between the two groups (P < 0.05)

TABLE (3) Comparison of implant stability at different follow up periods.

Osstell (ISQ)	Group I	Group II T-te		'-test
	Mean ± SD	Mean ± SD	t	P-value
Insertion	52.463 ± 3.537	51.835 ± 3.246	0.436	0.674
After 6 Months	54.53 ± 4.642	52.28 ± 4.543	0.433	0.885
After 12 Months	59.458 ± 3.785	53.54 ± 4.364	0.354	0.02*
After 24 Months	65.4 ± 4.366	55.7 ± 4.575	0.755	0.03*
After 36 Months	69.2 ± 4.569	57.8 ± 3.879	0.577	0.01*

^{*}Significance: P < 0.05

Marginal bone loss	Group I	Group II	T-test	
	Mean ± SD	Mean±SD	t	P-value
Insertion	0.95 ± 0.45	0.98 ± 0.65	1.57	0.536
After 6 Months	1.38 ± 0.53	1.46 ± 0.57	1.76	0.647
After 12 Months	1.67 ± 0.35	1.86 ± 0.43	1.48	0.03*
After 24 Months	1.79 ± 0.65	1.94 ± 0.59	1.65	0.01*
After 36 Months	1.82 ± 0.73	1.98 ± 0.76	1.73	0.02*

TABLE (4) Comparison of marginal bone loss at different follow up periods. (*Significance: P < 0.05)

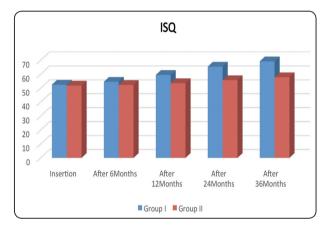


Fig. (5): Distribution of mean value of implant stability between the two groups at different follow up periods.

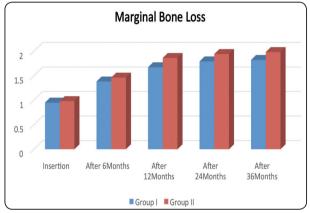


Fig. (6): Distribution of mean value of marginal bone loss between the two groups at different follow up periods.

DISCUSSION

Astringent glycemic control is important to be maintained to minimize diabetic co-morbidities¹⁷. However, a majority of diabetic persons still struggle with an inability to maintain adequate glycemic control ¹⁸, since diabetes mellitus remains a relative contraindication for dental implant therapy, depending upon the person's level of glycemic control ¹⁰.

Although evidence-based literature lacks information regarding immediate loading of dental implants in diabetic patients, this study provides reasonable supporting evidence to Ganeles et al ¹⁹ and Romanos et al ²⁰ that type II diabetes may not

be an absolute risk factor for immediate loading protocols.

Dental plaque contains microbes, such as Porphyromonas gingivalis (P. gingivalis), which significantly contribute to periodontal destruction ²¹. Inflammatory reactions in the periimplant tissues have been associated with the presence of dental plaque around implants ^{22,23}. Periodontal therapy has been shown to improve glycemic control in diabetic patients ²⁴.

A significant decrease in plaque index was observed through the three years of follow-up and attributed to routine hygienic recall visits. This matches the results of previous studies which

declared that following regular oral hygiene instructions resulted in successfully osseointegrated implants^{25,26}. This may explain the results form Ferreira and co-workers²⁷ where implants in diabetic patients with good glycemic control were found not to be associated with an increased risk of peri-implantitis when compared with non diabetic subjects.

It was also observed a slight trend of increasing probing depth around the implants during the followup periods. These findings could be attributed to bone resorption during the first year after implant placement; the increases were within acceptable values and are in agreement with previously reported results of a probing depth increase after one year follow-up period and explanation that this phenomenon of up to 1 mm marginal bone loss is related to maturation of bone after implant placement and adaptation of bone to withstand functional forces 28. The results of this study are also in agreement with the work from Turkyilmaz ⁹ who reported no pathological probing depth changes in patients with well-controlled Type II diabetic patients through one year follow-up period, and no evidence of diminished clinical success or significant complication related to implant treatment was found for this patient population.

Similarly, a slight trend of increasing marginal bone loss around the implants was observed during the follow-up periods. These changes match the results of recently published studies ^{29,30} concluding that patients with Type II diabetes can receive implant-based treatments with immediate loading safely, provided that they present with moderate HbA1c values indicative of good glycemic control. These results provide further support to Chrcanovic et al ²⁹ conclusion that the difference between the insertion of dental implants in non-diabetic and diabetic patients did not statistically affect the implant failure rates. The amount of bone level changes in this study was within the criteria for

implant success suggested by Albrektsson and coworkers ³¹.

Implant stability is a critical factor that determines the long-term success of dental implants ³². In this study, all the Osstell ISQ values are more than 50 and this indicates successful Osseointegration ³³.

A significant increase in the probing depth, marginal bone loss and implant stability was found after one year from overdenture insertion between the two groups. Our findings show that persons with HbA1c levels \geq 8% have compromises in implant stabilization that suggest alterations in the biologic integration of the implants in direct relation to glycemic control.

The findings of the current study are consistent with reports from previous studies that have demonstrated that hyperglycemic conditions lead to alterations in bone physiology ^{34, 35}. Impaired osseous healing in association with hyperglycemia has been demonstrated in several cross-sectional and retrospective studies ^{36, 37}.

The effects of a hyperglycemic state have been shown to include inhibition of osteoblastic cell proliferation and collagen production during the early stages of callus development, resulting in reduced bone formation, as well as diminished mechanical properties of the newly formed bone ^{35, 38}. The diminished bone formation may be exacerbated further by increased apoptosis of bone-lining cells in a hyperglycemic state³⁹. More recently, several animal studies have demonstrated a more persistent inflammatory response that may also lead to increased osteoclastic activity in a hyperglycemic state ^{40,41}.

Thus, the potential for alterations in bone metabolism in association with hyperglycemia is consistent with the longitudinal assessments of implant stabilization found in this study. Therefore, under optimal glycemic control, subjects with diabetes can have a periodontal bone height similar to that of healthy individuals.

In this study, the use of immediately-loaded flapless one-stage implants without a second surgical phase might be a reason of the success rate of the implants. The flapless implant surgery "minimally invasive" preserves maximum amount of blood supply to the bone. On the other hand, reflection of flap in the second stage will compromises part of blood supply coming from soft tissue to bone and interfere with the tissues vascularization ⁴².

Due to the limitations of this study, the authors suggest that longer evaluation period may be needed to assess the effect of glycemic control on implants survival in diabetic patients.

CONCLUSIONS

Wither the limitations of this short term study, glycemic control seems to have an effect on the survival of implants supporting complete overdentures in type II diabetic patients as it affect the crestal bone resorption and probing depth around implants and also affect implant stability.

REFERENCES

- King GL. The role of inflammatory cytokines in diabetes and its complications. J Periodontol 2008; 79(Suppl. 8):1527-1534.
- 2- American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2005; 28: 37-42.
- NIH. National Institutes of Health Consensus Development Conference statement on dental implants June 13-15, 1988. J Dent Edu. 1988: 52: 824–827.
- 4- Javed F, 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.
- 5- Cohen A, Horton ES. Progress in the treatment of type 2 diabetes: New pharmacologic approaches to improve glycemic control. Current Medical Research and Opinion. 2007; 23: 905–917.
- 6- Boltri JM, Okosun IS, Davis-Smith M, Vogel RL. Hemoglobin a1c levels in diagnosed and undiagnosed black, hispanic, and white persons with diabetes: Results from nhanes 1999–2000. Ethnicity and Disease. 2005; 15:562–567.

- 7- Wysham CH. New perspectives in type 2 diabetes, cardiovascular risk, and treatment goals.Postgraduate Medicine. 2010; 122:52–60.
- 8- Standards of medical care in diabetes. Diabetes Care. 2010; 33(Suppl 1):S11–61.
- 9- Turkyilmaz I. One-year clinical outcome of dental implants placed in patients with type 2 diabetes mellitus: A case series. Implant Dentistry. 2010; 19: 323–329.
- 10- Oates T, Huynh-Ba G, Vargas A, Peggy Alexander P, Feine J. A Critical Review of Diabetes Glycemic Control and Dental Implant Therapy. Clin Oral Implants Res. 2013; 24(2): 117–127.
- 11- Mombelli A, Lang N. Clinical parameters for the evaluation of dental implants. Periodontol 2000 1994;4:81-86.
- 12- Akagawa Y, Matsomoto T, Hashimoto M, Tsuru H. Clinical evaluation of the gingival around single crystal sapphire endosseous implant after experimental ligature induced plaque accumulation in monkeys. J Prosthet Dent 1992; 68:111-118.
- 13- Huang HM, Chiu CL, Yeh CY, Lin CT, Lin LH, Lee SY. Early detection of implant healing process using resonance frequency analysis. Clin Oral Implants Res 2003;14:437-443.
- 14- Capek L, Simunek A, Slezak R, Dzan L. Influence of the orientation of the Osstell® transducer during measurement of dental implant stability using resonance frequency analysis: A numerical approach. Med Eng Phys 2009; 31:764–769.
- 15- Mihoko A, Sang-Hoon P, Hom-Lay W. Methods used to assess implant stability status. The International Journal of Oral & Maxillofacial Implants 2007;22:743-754.
- 16- Walters RA. Vertical alveolar bone changes related to overdenture abutment teeth. J Prosth Dent 1987;57:309.
- 17- United Kingdom Prospective Diabetes Study (UKPDS) Group. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35). BMJ 2000;321:405-412.
- 18- Kirk JK, Bell RA, Bertoni AG, Arcury TA, Quandt SA, Goff DC Jr, et al. Ethnic disparities: control of glycemia, blood pressure, and LDL cholesterol among US adults with Type 2 diabetes. Ann Pharmacother 2005;39:1489-1501.
- 19- Ganeles J, Rosenberg M, Holt L, Reichman LH. Immediate loading of implants with fixed restorations in the completely edentulous mandible: report of 27 patients from a private practice. Int J Oral Maxillofac Implants 2001:16:418–426.

- 20- Romanos GE, Toh CG, Siar CH, Swaminathan D. Histologic and histomorphometric evaluation of periimplant bone subjected to immediate loading: An experimental study with Macaca fascicularis. Int J Oral Maxillofac Implants 2002;17:44-51.
- 21- Noiri Y, Okami Y, Narimatsu M, Takahashi Y, Kawahara T, Ebisu S. Effects of chlorhexidine, minocycline, and metronidazole on Porphyromonas gingivalis strain 381 in biofilms. J Periodontol 2003;74:1647-1651.
- 22- Javed F, Altamash M, Klinge B, Engstro"m PE. Periodontal conditions and oral symptoms in gutkachewers with and without type 2 diabetes. Acta Odontol Scand 2008;66:268-273.
- 23- Ma'ximo MB, de Mendoncxa AC, Renata Santos V, Figueiredo LC, Feres M, Duarte PM. Short-term clinical and microbiological evaluations of peri-implant diseases before and after mechanical anti-infective therapies. Clin Oral Implants Res 2009;20:99-108.
- 24- Heckmann SM, Heckmann JG, Linke JJ, Hohenberger W, Mombelli A. Implant therapy following liver transplantation: Clinical and microbiological results after 10 years. J Periodontol 2004;75:909-913.
- 25- Baraka O, Mohamed I. Clinical, Radiographic and Electromyographic evaluation of lingualized occlusion versus monoplane occlusion in implant-supported mandibular overdenture. Egy Dent J 2000;46:401-410.
- 26- Leonhardt A, Dahlen G, and Renvert S. Five-year clinical, microbiological, and radiographical outcome following treatment of peri-implantitis in man. J Periodontol 2003;74:1415-1422.
- 27- Ferreira S, Silva G, Cortelli J, et al. Prevalence and risk variables for peri implant disease in Brazilian subjects. J clin periodontol. 2006;33:929-935.
- 28- Visser A, Gerr M, Henny J, et al. Mandibular overdentures supported by two or four endosseous implants: A 5-years prospective study. Clin Oral Imp Res. 2005;16:19-25.
- 29- Chrcanovic BR, Albrektsson T, Wennerberg A. Diabetes and Oral Implant Failure: A Systematic Review. J Dent Res 2014;93:859-867.
- 30- Aguilar-Salvatierra A, Calvo-Guirado JL, González-Jaranay M, Moreu G, Delgado-Ruiz RA, Gómez-Moreno G. Peri-implant evaluation of immediately loaded implants placed in esthetic zone in patients with diabetes mellitus type 2: a two-year study. Clin Oral Implants Res. 2015 [Epub ahead of print].

- 31- Albrektsson T, Zarb G, Worthington P, Eriksson A. The long-term efficacy of currently used dental implants: A review and proposed criteria of success. Int J Oral Maxillofac Implants 1986;1:11–25.
- 32- Rabel A, Kohler SG, Schmidt-Westhausen AM. Clinical study on the primary stability of two dental implant systems with resonance frequency analysis. Clinical Oral Investigations 2007;11:257–265.
- 33- Sjostro"m M, Lundgren S, Nilson H, Sennerby L. Monitoring of implant stability in grafted bone using resonance frequency analysis. A clinical study from implant placement to 6 months of loading. International Journal of Oral and Maxillofacial Surgery 2005;34:45–51.
- 34- Funk JR, Hale JE, Carmines D, Gooch HL, Hurwitz SR. Biomechanical evaluation of early fracture healing in normal and diabetic rats. J Orthop Res 2000; 18:126-132.
- 35- Lu H, Kraut D, Gerstenfeld LC, Graves DT. Diabetes interferes with the bone formation by affecting the expression of transcription factors that regulate osteoblast differentiation. Endocrinology 2003; 144:346-352.
- 36- Loder RT. The influence of diabetes mellitus on the healing of closed fractures. Clin Orthop Relat Res 1988; 232:210-216.
- 37- White CB, Turner NS, Lee GC, Haidukewych GJ (2003). Open ankle fractures in patients with diabetes mellitus. Clin Orthop Relat Res 414:37-44.
- 38- Amir G, Rosenmann E, Sherman Y, Greenfeld Z, Ne'eman Z, Cohen AM. Osteoporosis in the Cohen diabetic rat: correlation between histomorphometric changes in bone and microangiopathy. Lab Invest 2002; 82:1399-1405.
- 39- He H, Liu R, Desta T, Leone C, Gerstenfeld LC, Graves DT. Diabetes causes decreased osteoclastogenesis, reduced bone formation, and enhanced apoptosis of osteoblastic cells in bacteria stimulated bone loss. Endocrinology 2004; 145:447-452.
- 40- Liu R, Bal HS, Desta T, Behl Y, Graves DT (2006). Tumor necrosis factoralpha mediates diabetes-enhanced apoptosis of matrix-producing cells and impairs diabetic healing. Am J Pathol 2006; 168:757-764.
- 41- Kayal RA, Tsatsas D, Bauer MA, Allen B, Al-Sebaei MO, Kakar S, et al. Diminished bone formation during diabetic fracture healing is related to the premature resorption of cartilage associated with increased osteoclast activity. J Bone Miner Res 2007; 22:560-568.
- 42- Al-Juboori MJ, Bin Abdulrahaman S, Jassan A. Comparison of flapless and conventional flap and the effect on crestal bone resorption during a 12-week healing period. Dent Implantol Update. 2012; 23: 9-16.