Bone augmentation as an adjunct to dental implant rehabilitation in patients with diabetes mellitus: A review of literature

ABSTRACT
The aim of the present article is to review the success of bone augmentation performed as an adjunct to dental implant rehabilitation in patients with diabetes mellitus. A literature review was conducted in PubMed on this topic, which yielded a total of 102 publications. For inclusion, publications had to be human studies, written in English language and should report on the success of bone augmentation as an adjunct to dental implant rehabilitation in diabetic patients. After screening the titles and abstracts, 11 full texts publications were obtained, of which seven were included in the review. These studies provided data on various bone augmentation techniques such as sinus floor elevation (SFE), guided bone regeneration (GBR), and onlay bone grafting. Even though the current review revealed that there are not many studies reporting data relevant to the analyzed topic, the data obtained suggests that; (1) staged GBR technique should be considered more feasible and predictable for bone augmentation, (2) clinicians must take meticulous care when planning and conducting SFE, and (3) block bone augmentation technique should be avoided.

Keywords: Guided bone regeneration, onlay bone graft, sinus floor elevation

INTRODUCTION
Dental implants are being increasingly used for replacement of missing teeth. Dental implant therapy in patients having diabetes mellitus (DM) is still considered a relative contraindication because of the increased susceptibility to infections, impaired wound healing, and associated microvascular complications. However, they do not encounter a higher implant failure rate than the normal population, if the plasma glucose levels are normal or close to normal. Data from the published retrospective and prospective studies indicated that the success rate of dental implants in diabetic patients were in the range of 85.5%–100% and were comparable to the nondiabetic patients.

Successful implant therapy is dependent on an adequate volume of bone at the site of implant placement. As DM is associated with increased rate of periodontal disease and bone loss compared to healthy individuals, a common problem encountered while placing implants is the lack of sufficient bone volume. Despite this fact, an increasing number of diabetic patients are being rehabilitated for missing teeth with dental implants, which may require bone grafting procedure.

However, limited studies have evaluated the success of bone augmentation in patients with DM. The clinicians are still uncertain about the safety and predictability of bone augmentation procedures in these patients. The present article, therefore, aims to review the success of bone augmentation as an adjunct to dental implant rehabilitation in patients with diabetes mellitus: A review of literature.

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augmentation performed as an adjunct to dental implant rehabilitation in patients with DM.

METHODS

The inclusion and exclusion criteria were already defined by the authors. For inclusion, publications had to be human studies and should be written in English language. Every study design (prospective, retrospective and randomized controlled trial [RCT]) was accepted. Publications had to assess the success of bone augmentation as an adjunct to dental implant rehabilitation in diabetic patients either before implant placement or within 6 months of implant placement. The intervention considered in the review involved bone augmentation in patients with DM. Even if studies did not adopt the same criteria, the success of bone augmentation as an adjunct to dental implant rehabilitation was the main outcome. However, in studies where the success of bone augmentation was not clearly mentioned, overall survival rates of dental implants in the bone augmented sites were considered. Publications reporting failure as; complete or partial loss of bone graft material (graft exposure), graft which had to be removed or regrafted, failure of vascularization, the interposition of fibrous tissue between the graft and the recipient site, inability to place implant and loss of implant in augmented sites were included in the review.\[11,13-16\] Publications by same authors reporting similar data in later publications and any irrelevant publications were excluded. The studies describing implant survival rate in nonaugmented sites were also excluded.

The search strategy incorporated a search of the electronic database, supplemented by cross-checking of the references of relevant articles. A literature search was conducted in PubMed up to September 2016 in accordance with the preferred reporting items for systematic reviews and meta-analysis statement, using the search terms: “success,” “outcomes,” “bone grafts,” “bone augmentation,” “bone regeneration,” “alveolar bone grafts,” “alveolar bone regeneration,” “alveolar bone augmentation,” “diabetes” “oral implant,” and “dental implant.”

A screening process was undertaken independently by two reviewers (KL and AS) [Figure 1]. At first, all titles were screened to eliminate irrelevant publications, review articles, case reports, case series, in vitro studies, animal studies, and non-English language publications. Then, all abstracts of the selected articles were screened and studies were excluded on the basis of patient characteristics, intervention, and outcome characteristics. The full texts of relevant articles were analyzed based on the inclusion and exclusion criteria.

Any disagreements between the two reviewers were resolved after additional discussion with a third reviewer (BT).

RESULTS

The preliminary search from the PubMed database resulted in 102 articles. After screening the titles, 32 potentially relevant articles were identified, and then, after screening the abstracts, 11 full text publications were obtained and analyzed. The cross-references of the publications were also checked. Finally, all relevant seven publications which fulfilled the inclusion criteria were considered in the present review. The review includes only prospective and retrospective studies because of the absence of RCTs and controlled clinical trials. Furthermore, due to the heterogeneity between studies, the synthesis of data is presented narratively. A table was created to organize the data obtained from all the included studies [Table 1].

LITERATURE REVIEW

Balshi et al. evaluated the success of 227 dental implants in 34 diabetic patients. Bone grafting was done at 31 of the 227 sites, of which one grafted site (3.2%) failed. Autogenous bone and a membrane were used at this site. At second-stage surgery, 13 implants out of the 227 failed to osseointegrate, a survival rate of 94.3%. A clinical survival rate of 99.9% was reported with only one implant failure among the 177 implants.
that were followed through final restoration. This implant was placed in a grafted site in left maxilla and failure occurred due to occlusal overload caused by bruxism.10

Farzad et al. in their retrospective study reported installation of dental implants in 782 patients out of which 25 patients were diabetic (both type 1 and type 2). A total of 136 implants were placed in these 25 diabetic patients. Three implant sites required the bone grafting procedure. The type of bone grafting was not mentioned, but the results of the study reported that none of the three grafted sites failed or developed any complications. They concluded that diabetics that undergo dental implant treatment, including bone grafting, do not encounter a higher implant failure rate than normal population if the patients’ plasma glucose levels are normal or close to normal.5

Schwartz-Arad et al. evaluated the success of intra-oral autogenous block onlay bone grafting (OBG) for alveolar ridge augmentation. Out of the 56 patients included in

| Author(s)                      | Publication year | Study design | Total number of patients/diabetic patients | Total number of bone grafted sites in the study | Total number of implants placed in bone grafted sites in the study | Type of bone augmentation technique/bone graft material | Simultaneous/2-staged implant placement | Success rate of bone augmentation/survival rate of implants |
|--------------------------------|-----------------|--------------|--------------------------------------------|-----------------------------------------------|---------------------------------------------------------------|------------------------------------------------|-------------------------------------|----------------------------------------------------------|
| Balshi and Wolffinger10        | 1999            | Retrospective | 34/34                                      | 31                                            | 31                                                            | Autogenous bone and a membrane. Type of technique and site of placement not mentioned | Simultaneous                                      | Of the 31 grafted sites, one (3.2%) failed               |
| Farzad et al.5                | 2002            | Retrospective | 25/25                                      | 3                                             | Not mentioned                                                | Not mentioned Autogenous block OBG                  | -                                   | 100% of the implants in 3 diabetic patients. 25% success rate in DM |
| Schwartz-Arad et al.11        | 2005            | Retrospective | 56/4                                       | 64 grafts placed for later dental implant    | Not mentioned                                                | Autogenous block OBG                               | -                                   | -                                                       |
| Tawil et al.12                | 2008            | Prospective  | 45/45                                      | -                                             | 54                                                           | 34 implants with SFE and 20 implants with GBR           | Simultaneous                                      | Implant success rate of 91.1% with SFE and 85% with GBR. Overall, implant survival rate of 97.2% in diabetics |
| Huynh-Ba et al.13             | 2008            | Retrospective | 136/7                                      | 116 (9 in diabetics)                         | -                                                            | SFE (one or two-step antrostomy or the osteotome technique) with bovine bone graft/a bio absorbable collagen membrane | Simultaneous/staged                           | Overall implant survival rate in the study was 92.2% in SFE group |
| Kaing et al.14                | 2011            | Retrospective | 75/1                                       | 86 bone grafts as an adjunct to dental implants | -                                                            | Particulate and block grafts (autogenous and bone substitute material) | Assessment of bone graft success was made at 3 months | Total 10 graft failures. 1 failure in a patient with DM |
| Erdogan et al.15              | 2015            | Prospective  | 24/12                                      | -                                             | 43 (22 in diabetics and 21 in nondiabetics)                   | Staged GBR with mixture of autogenous bone and synthetic bone substitute plus collagen membrane | 2-staged - implant placement 5 months after bone grafting | Survival rate of implants was 100%                      |

GBR: Guided bone regeneration, SFE: Sinus floor elevation, OBG: Onlay bone grafting, DM: Diabetes mellitus
the study, four patients had diabetes, and all of them had complications subsequent to the OBG procedure. In three, out of the four patients, bone graft failure (i.e., graft exposure) occurred. OBG was performed 5.2 ± 1.1 months before implant placement, i.e., delayed implant placement or a two-stage procedure was followed in the study. According to the results of the study, intraoral block bone grafts were not recommended for diabetic patients due to significantly higher failure rates and more post-operative complications.¹¹

A prospective study by Tawil et al. evaluated implant and alveolar bone augmentation success rates in patients with type 2 DM. A total of 255 Branemark implants were placed in 45 type 2 diabetic patients. Of the 45 patients, 22 patients were well-controlled diabetic (HbA1c <7%), 22 patients belonged to the fairly controlled diabetic group (HbA1c 7% to 9%) and only one patient was poorly controlled diabetic (HbA1c >9%). They placed ten implants following sinus floor elevation procedure (SFE) and six implants following guided bone regeneration (GBR) in patients with well-controlled diabetes. In patients with fairly controlled diabetes, 24 implants were placed following SFE and 14 with GBR. 143 implants were placed following a conventional protocol, wherein adequate bone volume was present. The success of bone augmentation technique in the present study was evaluated on the basis of overall survival rates of dental implants. Although they reported no significant difference in implant survival between conventional and advanced therapy groups (i.e., after SFE and GBR), three implant failures were reported with each of the bone augmentation procedure.¹²

A retrospective study by Huynh-Ba et al. assessed predictors for implant failure in the posterior maxilla which included gender, diabetes, smoking, implant length, implant diameter, membrane use, sinus-elevation technique, and surgical complications. They had placed a total of 273 implants; 116 implants with SFE technique and 157 implants in native bone. Of these, 19 implants were placed in patients with well-controlled diabetes; 9 implants following SFE and 10 implants in native bone. Overall in the study, the implants that were placed in SFE group showed more failures than the native bone group, but the difference was not statistically significant. With regards to complication rate, the SFE group had more complications than the native bone group, and the difference was statistically significant. SFE procedures with simultaneous or staged implant placement and diabetes did not increase the risk for implant failure in the present study, whereas smoking and surgical complications had a statistically significant effect on implant failure. However, the procedure should be carried out with utmost care in diabetic patients to avoid complications.¹³

Kaing et al. evaluated the outcome of bone grafts placed as an adjunct to implant rehabilitation and assessed the factors affecting the survival of these grafts. A total of 86 bone grafts were placed using lateral augmentation, open sinus lift, closed sinus lift, and ridge split augmentation techniques. Types of grafts were particulate and block bone (autogenous and mixed autogenous/bone substitute material). All the grafts that failed in the study were block bone type. The factors which significantly increased graft failure included the use of bone block augmentation, mixed autogenous/bone substitute grafts, and DM. This retrospective study concluded that care should be taken when planning block grafts in diabetic patients. Anterior recipient site for bone graft placement approached significance with a trend of increased failure rates.¹⁴

Erdogan et al. conducted a prospective clinical study to determine the outcome of dental implant therapy with staged GBR procedures in type 2 diabetic patients. Twenty-four patients were included in the study. Half of the patients were diagnosed with the type 2 DM (Group 1), whereas the other half (Group 2) included nondiabetic patients. The staged GBR procedure was carried out with 50%–50% mixture of autogenous bone and synthetic bone substitute plus collagen membrane. Patients were recalled 5 months after bone augmentation surgery for implant placement. Prosthetic treatment was carried out 4 months after implant placement. There was no significant difference between the two groups in terms of alveolar bone width gain, wound healing scores, implant stability scores, and marginal bone loss values. The survival rates of implants were 100% for both the groups. The success rate of implants was 95% for Group 1 and 100% for Group 2. The study concluded that staged GBR is a feasible augmentation procedure for the treatment of horizontal bone deficiencies of the maxillary anterior/premolar regions in well-controlled type 2 diabetic patients.¹⁵

**DISCUSSION**

The aim of the present article is to review the success of bone augmentation performed as an adjunct to dental implant rehabilitation in patients with DM. Due to the absence of appropriate RCTs, this review included only prospective and retrospective studies.

As tooth loss results in decreased bone volume and width, it may necessitate the need for bone augmentation in deficient areas either before implant placement (2-staged protocol) or if primary stability can be achieved, then at the time of implant placement (simultaneous protocol).¹⁴ The success of bone augmentation procedure predominantly relies on
the type of bone graft material used and on the type of bone augmentation technique employed.

FACTORS THAT IMPEL THE SUCCESS OF BONE AUGMENTATION AS AN ADJUNCT TO DENTAL IMPLANT REHABILITATION IN PATIENTS WITH DIABETES MELLITUS

Bone augmentation technique
From the present literature review, it can be concluded that intraoral autogenous block bone augmentation is not recommended for diabetic patients as DM has significantly increased risk of graft failure in such cases.[11,14] Block grafts, though, preserve bone volume better than particulate grafts, revascularization, especially in mandibular block grafts is slow. A systematic review by Wallace and Fromou also found that block grafting resulted in a lower implant survival rate than particulate grafts.[17] Studies can be carried out to determine how to conduct an OBG procedure in diabetic patients with minimal risk of graft failure.

The SFE procedures with autogenous or bovine bone grafts did not increase the risk of graft failure (or implant failure) in patients with DM, however, significantly increased rate of complications have been reported in SFE group when compared to native bone group irrespective of the systemic status of the patients.[13] Therefore, the clinician must take meticulous care when planning and conducting SFE in diabetic patients.

The use of GBR, simultaneous or staged, for bone augmentation in diabetics has met with a success rate of 85% and 95%, respectively, which can be considered acceptable in the context of current dental implantology literature.[12,15] The combination of GBR with autogenous/bovine/synthetic bone substitutes and the membrane has been studied.[15,18] Although the use of autogenous bone for augmentation is considered as gold standard, it has several disadvantages.[16,18] To avoid the use of autogenous bone with GBR, Hammerle studied the success of horizontal bone augmentation with deproteinized bovine bone mineral (DBBM) and a resorbable bone membrane. They concluded that a combination of DBBM and resorbable collagen membrane was an effective treatment option before implant placement. Although they did not include diabetic patients in their study, this bone augmentation technique can be applied in diabetics as it offers several advantages such as: (i) Use of autogenous bone is avoided (ii) following regeneration, no extensive raising of flaps is necessary for membrane removal, (iii) no exposure of the regenerated bone in the apical areas, (iv) additional advantage of resorbable membranes, and (v) decreased patient morbidity.[18] To summarize, staged GBR technique can be considered a feasible bone augmentation procedure in patients with diabetes. Further studies can be conducted to evaluate the outcomes of GBR technique with synthetic bone substitutes or DBBM and resorbable collagen membrane in diabetics.

Diabetic status and duration
Good glycemic control (HbA1c < 7%) is essential to minimize complications associated with bone augmentation and implant placement procedures. The studies discussed in this review included patients with well-controlled DM, except in one study by Tawil et al. which included patients with well-controlled, fairly controlled, and poorly controlled diabetes. The same study showed no effects of the duration of diabetes on the survival of implants or on the occurrence of complications such as peri-implantitis.[12] On the contrary, Olson et al. investigated effects of the duration of diabetes on implant success and concluded that implant success is significantly associated with the duration of the diabetic history.[19] Further studies need be conducted to evaluate the success of bone augmentation techniques in patients with fairly controlled diabetes and also to obtain definitive conclusions with regards to the effect of duration of diabetes.

Bone graft recipient site and donor site
Complications at the recipient site which might lead to graft failure include infection, wound dehiscence, hematoma, and swelling. Schwartz-Arad et al. reported no relation between complications or failure rates and the donor and recipient sites (i.e., maxilla, mandible, anterior, and posterior).[11] Erdogan et al. in their study harvested autogenous bone from mandibular molar/retromolar region for augmentation of maxillary anterior or premolar regions. They scored, wound healing at both recipient and donor sites and reported no significant differences in healing between the diabetic and control group for both the sites.[15] Kaing et al. reported 10 graft failures at recipient sites; 8 failures in the anterior maxilla and 2 failures in the posterior maxilla. They concluded that anterior recipient site for bone graft placement approached significance with a tendency toward increased failure rates.[14]

Timing of implant placement and implant loading
Implants can be placed simultaneously with bone grafting or as two-stage procedure. Simultaneous or immediate implant placement exposes the patient to some risks, such as partial or total loss of the graft, membrane, or graft exposure and/or infection.[16] A two-stage procedure, i.e., delayed implant placement would be more predictable in diabetics as it allows sufficient time for graft healing, consolidation, and revascularization.[16] The studies that adopted staged implant placement allowed an average graft healing period of 5 months.[11,13]
It is has been found that as patients with diabetes have slow rate of bone remodeling, it is suggested to delay implant exposure by 4–8 weeks than the routine duration which has been found acceptable for the general population. For this reason, it was suggested that immediate loading of implants should be avoided in diabetic patients. Erdogan et al. adopted a delayed loading protocol and reported 100% implant survival rate and 95% implant success rate in diabetics.

Habit of smoking
Smoking and DM are risk factors that can significantly affect the outcomes of dental implants and bone grafts. Studies have demonstrated significantly higher failure rates of bone augmentation and increased incidence of postoperative complications in smokers. Diabetic patients should be counselled to quit their habit of smoking, and if not accomplished, it is suggested that bone augmentation procedures should be carefully planned to ensure uncomplicated treatment outcomes.

Oral hygiene
Poor oral hygiene is another controllable risk factor that can significantly influence the outcome of bone grafting procedures. Patients must be made to follow and maintain a meticulous oral hygiene régime to prevent complications or failures. The use of 0.12% chlorhexidine mouthwash has shown a clear benefit in type 2 diabetic patients by reducing the failure rates from 13.5% to 4.4%, during a follow-up period of 36 months. This study also observed a reduction of 10.5% in the implant failure rate when antibiotics were administered preoperatively.

CONCLUSION
Within the limitations of the present review, from the clinical point of view, the following conclusions can be drawn with regards to success of bone augmentation as an adjunct to dental implant rehabilitation in diabetic patients: (1) DM cannot be considered as a contraindication to implant-related bone augmentation procedures if the patient is maintaining a good glycemic control, (2) staged GBR technique should be considered more feasible and predictable for bone augmentation, (3) clinicians must take meticulous care when planning and conducting SFE, and (4) block bone augmentation technique should be avoided. RCTs should be conducted to enable formulation of set guidelines with regards to successful bone augmentation procedures in well-controlled or fairly controlled diabetic patients for dental implant rehabilitation.

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Conflicts of interest
There are no conflicts of interest.

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