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EVALUATION OF BONE TURNOVER MARKERS AS INDICATORS FOR OSSEOINTEGRATION OF DENTAL IMPLANTS (A CLINICAL TRIAL)

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ABSTRACT

BACKGROUND: Dental implants are considered a highly reasonable method for the replacement of missing teeth and the success of this treatment modality is highly dependent on the bone quality; where the better the quality the more superior the implant osseo-integration. Bone turnover process also plays a fundamental role in implant osseo-integration and can give a prediction of the future implant stability and possible bone loss when its blood markers are assessed.
OBJECTIVE: To assess the bone turnover marker (BTM) values and correlate their impact on the condition of the jaw bone in patients having dental implants and to evaluate the density and quality of bone around the implant radiographically in relation to normal and abnormal bone turnover markers.
MATERIAL AND METHODS: This study was carried out as a single arm clinical trial. Fifteen male patients who require single tooth replacement in the lower posterior region, whose age range was 30-40 years, underwent blood analysis of bone turnover markers; bone alkaline phosphatase and osteocalcin, using the technique of ELISA and CBCT examination preoperatively. The bone density was measured in the proposed area of implant placement using Ondemand software. Following implant placement bone density and marginal bone loss were radiographically evaluated 3 and 6 months postoperatively and the results were correlated to the patient's bone turnover markers values.
RESULTS: There was maximum primary stability and successful osseo-integration in all implants, with minor reduction in the bone density before and after the implant placement as well as minor marginal bone loss after 6 months of follow-up, but both were statistically non-significant. There was no significant correlation between marginal bone loss and abnormal bone turnover values.
CONCLUSION: Bone turnover markers could not be used to evaluate the bone condition prior to referring to dental implant treatment thus they are not indicators of implant's osseo-integration.
KEYWORDS: Bone turnover, bone quality, dental implants, osseointegration.
RUNNING TITLE: Evaluation of BTM to assess dental implants osseo-integration.

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INTRODUCTION

There is a variety of treatment options for the replacement of missing teeth, among which is the dental implant (1). The dental implant is a biocompatible and biofunctional permucosal device that is placed on or within the jaw to provide support for removable or fixed prosthesis. They are screw-like posts made from titanium and surgically drilled into the jawbone to replace the tooth root thus improving function and enhancing the overall appearance. (2, 3).
The success rate of implant treatment is dependent on efficient osseo-integration by which the implant is perfectly integrated inside the bone. The better the osseo-integration, the higher the success rate (4).

Bone quality assessment is of prime importance prior to dental implant treatment, as it is reflected on the implant survival rate (5). Bone quality can be defined as "The sum of all bone properties that affects the bone fracture resistance". Based on the National Institute of Health, it is specifically related to the bone turnover, architecture, mineralization and micro-damage's accumulation (6). Accordingly type IV bone quality (soft bone) is the least liable to osseo-integrate owing to decreased bone mineral density (7).
Since jawbone density is strongly correlated to skeletal bone density, using a biochemical method of monitoring bone metabolism can give us an

indication of the current bone quality and mineral bone density (7,8).

Bone turnover markers (BTMs) are a group of protein or protein derivative biomarkers released by osteoclasts or osteoblasts during the process of bone remodeling. They represent a very promising tool in monitoring bone turnover (9).

The use of BTM to provide sensitive and specific assessments of the of the skeletal bone metabolism rates has widely spread nowadays. This method requires measuring the proteins and enzymes released during formation of bone and as well as the break down products produced during bone resorption which are eventually bone density related (10).

Recent studies showed that decreased bone mineral density is associated with increased values of both resorptive and formative markers (11). These measurements can be also aided by the use of x-ray examination particularly in the field of implant dentistry (5,12). Thus BTMs can offer prognostic information of the implant osseointegration.

The value of BTMs is influenced by a variety of factors, which can either maintain it within the normal limits or induce extremes of values beyond the normal, including gender, age, circadian rhythms, menstrual cycle, fasting or non-fasting, exercise and medical condition (13).

Since bone quality assessment prior to dental implant treatment is challenging to assure, we relied on bone turnover markers' values as indicators of the bone quality.

The null hypothesis will be that there is no difference between normal and abnormal bone turnover values on the bone density as well as on the dental implant osseo-integration.

The study aimed to assess the bone turnover marker values and correlate their impact on the condition of the jaw bone in patients having dental implants and to evaluate the density and quality of bone around the implant radiographically in relation to normal and abnormal bone turnover markers.

MATERIAL AND METHODS

The study was performed as a single arm (before and after) clinical trial, carried out upon approval of the Committee of Research Ethics at the Faculty of Dentistry, Alexandria University, on -20/6/2021. Ethics Committee No. 0254-06/2021.

Prior to the procedure, all patients signed an informed consent form at the Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Alexandria University, to ensure they fully understand the procedure's outcome, benefits and possible risks.

Sample size estimation was based on the following assumptions:

- α error, Probability of chance (not more than 5%) and a confidence level= 95%.
- β error (20%) and study power= 80%.

The proposed minimal sample size was 13 patients (as stated by the statistician and in reference to Yasuda et al. (14) who conducted a previous similar study. In order to reduce the probability of drop-out through the treatment strategy, 10% was added to the sample size from the beginning of the study according to the Oxford statistical standards.

Therefore, fifteen patients who require prosthodontic implants were recruited from the outpatient clinic, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Alexandria University. This trial was designed and reported following the CONSORT guidelines (15).

Eligibility criteria

The selection of the candidates was based on certain inclusion and exclusion criteria.

Inclusion Criteria

1. Male patients having a partially edentulous lower ridge for at least 3 months, suitable for single tooth replacement by dental implant at the site of lower posterior region.
2. Age range from 30 to 40 years.
3. Good oral hygiene (plaque index < 20%) (16,17).

Exclusion Criteria

1. Recent extraction less than 3 months.
2. Heavy smokers (≥25 cigarettes).
3. Systemic diseases like uncontrolled diabetes, arthritis, hypothyroidism, hyperparathyroidism and osteoporosis.
4. Bone grafts in the proposed implant site (18).

Material

1. Dental implant (Neobiotech, internal connection system, Korea)
2. Dental motor (X-CUBE, Saeshin, Korea)
3. Osstell ISQ and Smartpeg (Goteborg, Sweden).

Methods

Preoperative Phase

Patient clinical examination

A detailed medical and dental history were obtained from each patient along with complete blood picture. Each patient was clinically examined to verify the presence of the following: good periodontal status, proper occlusion, enough edentulous space mesio-distally between the neighboring teeth and enough inter-arch space to accommodate the future crown. (19)

Patient radiographic examination

Each patient had undergone a cone beam computed tomography (CBCT) scan. The data was stored in DICOM format and opened using implant planning software (Ondemand). Using this software, the corresponding implant sites were evaluated through different angulations and cross sectional cuts.

Measurement of bone density

At the proposed implant placement sites, the bone density was measured on the mesiodistal and buccolingual cross-sectional CBCT slices in Hounsfield units (HU) by selecting region of interest (ROI), which is one of the tools used in the

software measurements to automatically calculate the bone density. The bone density was measured both bucally and lingually and the mean of both measurements was used as the cancellous bone density at the proposed area (16). **(Figure 1)**

Patient laboratory examination

The bone turnover analysis was attempted only preoperatively. Beside the bone turnover markers analysis, complete blood picture was obtained from each patient. The sample was taken from all patients in the early morning between 8 and 10 am. The patients were advised to be fasting and to avoid any physical exercise 24 hours prior to the sampling as recommended (20).

BTMs are divided into both formative and resorptive ones (16). The study was concerned with the measurement of bone formation markers including osteocalcin (OC) and bone alkaline phosphatase (BAP).

Osteocalcin (OC)

OC is one of the proteins exclusively produced by hypertrophic chondrocytes, osteoblast and odontoblasts. OC is considered one of the primary proteins associated with the process of bone remodeling and its action production is regulated by negative feedback mechanism. through the detection of minor fractions released into the circulation by immunoassays. Many studies suggest that osteocalcin is released mainly during formation but it can be also detected in the circulation during bone resorption as well (21).

Bone alkaline phosphatase (BAP)

BAP is membrane-bound tetrameric enzyme involved in osteoid formation and mineralization. It is considered a highly reliable, inexpensive and simple method of measuring bone metabolism and providing an impression of the osteoblast activity and new bone formation (22, 23).

Methodology of bone turnover analysis

In this study bone turnover markers were analyzed preoperatively, using the technique of enzyme-linked immunosorbent assay (ELISA).

ELISA is a plate-based assay technique designed to detect and quantify antibodies, proteins, hormones and peptides. In this technique, immobilization of an antigen to a solid surface takes place which is then adjoined with an antibody that is enzyme linked. The detection process is achieved by assessing the activity of the conjugated enzyme through incubation with a substrate to produce a measurable product. This specific antigen-antibody interaction is most important element of such detection strategy (24).

The results obtained using ELISA gives a precise diagnosis of a particular disease or condition since it uses two antibodies. The technique of ELISA is highly recommended for complex samples as the detection doesn't require antigen purification. Since it utilizes both direct and indirect methods of analysis it is considered a highly responsive and rapid test for the assessment of BTMs (24).

The mean reference range for each bone turnover marker in healthy individuals was set to all taken samples as follows: bone alkaline phosphatase 3.7–20.9 ng/ml and osteocalcin 2.5–13.0 ng/ml; for men.

Specimen collection

The analysis of bone turnover markers requires a sample of 50 mL of human serum or plasma using ELISA. After sample collection the blood was left to clot at room temperature for 30 minutes before the serum separation by centrifugation (900 – 1500 rpm for 10 minutes). The separation of the serum from the clot as achieved within three hours of blood collection and transferred to a clean test tube. The storage temperature of the Serum sample was -20°C until measurement, where all collected samples were analyzed at once (25).

Surgical Phase

Chlorhexidine mouthwash 0.12% was used by the patients, 30 minutes before the operation. Local anesthesia was administered with a concentration of 2% Lignocaine and 1:200,000 adrenaline which was preceded by 5% povidone-iodine solution antiseptic preparation of the operative site. (26)

A conventional envelope flap was made using scalpel blade number 15 then using a periosteal elevator, the flap was reflected to expose the alveolar ridge at which the implant was placed. **(Figure 2 b) (Figure 3 b, c)** Cortical and pilot drill was first used incorporated with length adjustor, followed by the next width increasing drills corresponding to the chosen implant diameter. **(Figure 2 c) (Figure 3 d)** The parallelity of drilling was checked using paralleling pin. **(Figure 2 d) (Figure 3 e)**

Then the implant was inserted at the drilled hole using the fixture driver. **(Figure 2 e, f) (Figure 5 a)** The implant was screwed into place to the full length using the torque ratchet. (27) (**Figure 2 g) (Figure 5 b)**

The implant stability was calculated using Osstell device which was placed in close proximity to the SmartPeg that was screwed into the implant's internal thread. (**Figure 4 a)** The Osstell emits magnetic pulses that cause the SmartPeg to resonate. At a distance of around 2-3 mm the measurement was made at right angle, and 3 mm superior to the soft tissue. The measurements were performed in the buccal, lingual, distal and mesial directions for each inserted implant. These measurements were taken twice and the mean in all directions was recorded as the implant representative ISQ (22). **(Figure 4 b, c)**

The cover screw of the implant was inserted using the screw driver. **(Figure 4 d) (Figure 5 d)**

The osseointegration rigidity and implant lateral stability determine the degree of resonance which was interpreted using resonance frequency analysis (RFA) (22).

The surgical site was debrided and irrigated with 0.9% normal saline, followed by 3/0 black silk suturing. **(Figure 4 e) (Figure 5 e)**

Following a recuperation period of four to six months, to ensure that the implant was well osseo-integrated and is ready to withstand various occlusal and masticatory forces, the phase of prosthetic rehabilitation was initiated. Experienced

prosthodontists had performed the prosthetic rehabilitation. (3, 28)

Postsurgical Phase

Postoperative instructions included a postoperative dose of Amoxicillin with Clavulanic acid 1g tablet, two times a day for five days. Ibuprofen 400 mg tablet was also prescribed three times a day for 3 days, as a pain reliever. The patients were scheduled for follow up on the 3rd and 6th month postoperatively. Sutures were removed after 7 days. **(Figure 4 f) (Figure 5f)**

Follow-Up Phase

Study outcomes

1. **Clinical outcome**

Implant stability during the follow up was an indication of optimum osseo-integration, which was re-evaluated using Osstell device two weeks and four weeks postoperatively.

2. **Radiographic outcome**

Radiographic Variables

Marginal bone loss calculation

During the follow-up observation phase, the marginal bone loss (MBL) was radiographically measured utilizing Ondemand CBCT 3D® software (CyberMed, Finland) (29).

The measurements were based on reference points which included:

a. The implant tip.
b. The horizontal connection between the abutment and the implant which was defined as the implant platform.
c. The first implant-bone contact (FIBC) (14). **(Figure 6)**

The distance from the FIBC to the implant platform was considered as the level of marginal bone.

The level of the marginal bone was recorded in mm using the ratio of the existing implant height and the distance from the implant tip to the implant platform on the images. MBL were measured as the difference in the marginal bone level immediately after the surgery and at the follow-up period three and six months postoperatively. The mean MBL values of distal and mesial sides were used for the study. **(Figure 6)**

Remeasurement of bone density

The bone density was remeasured by selecting Region of Interest (ROI) from the tools. The bone density was measured at three different points around the dental implant; in the middle of the mesial surface, in the middle of the distal surface and apically in the middle of the implant tip. The average of these calculations were recorded as the bone density. These measurements were made for all patients at the 3rd month postoperatively and repeated at the 6th month follow up (30). **(Figure 6)**

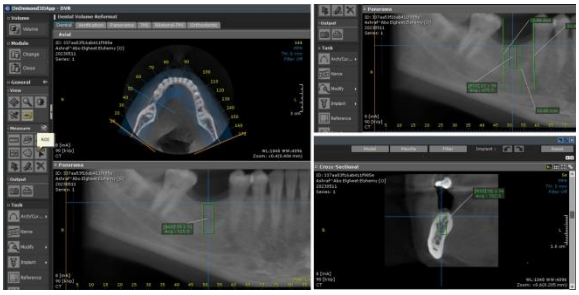

Figure (1): Measurement of bone density on the mesiodistal and buccolingual cross-sectional CBCT slices in Hounsfield units by selecting region of interest (ROI).

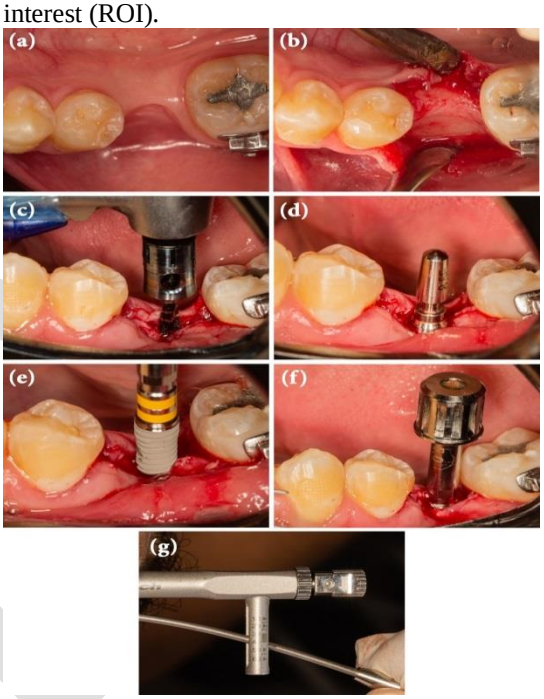

Figure (2): a) Preoperative, b) Flap incision and reflection, c) Drilling using Cortical and pilot drill incorporated with a length adjustor, d) Parallelity of drilling was checked using paralleling pin, e,f) implant insertion using fixture driver, g) Implant screwed into place to the full length using the torque ratchet.

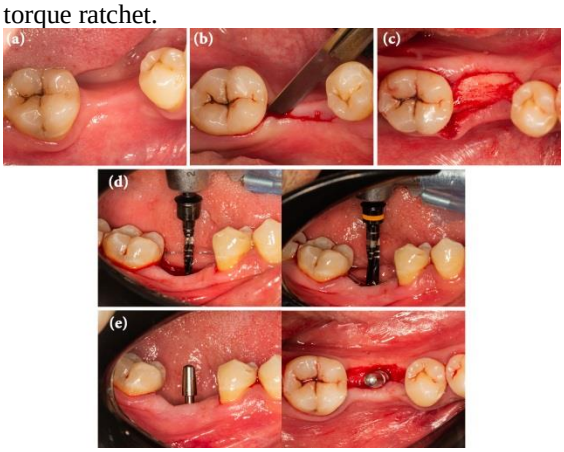

Figure (3): a) Preoperative, b) Flap incision, c) Flap reflection, d) Drilling using Cortical and pilot drill incorporated with a length adjustor followed by width increasing drills, e) Parallelity of drilling

was checked using paralleling pin.

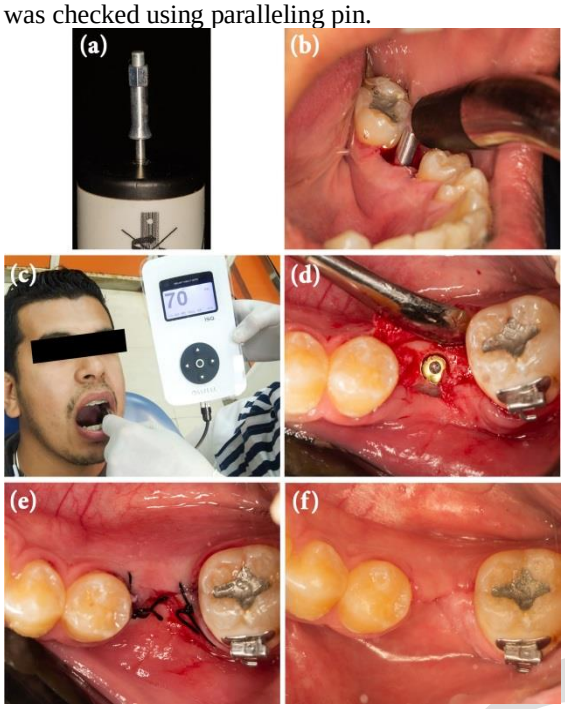

Figure (4): a) SmartPeg, b) Implant stability measured using Osstell device placed in close proximity to the SmartPeg, c) Implant representative ISQ shown on the Osstell monitor indicating primary stability d) cover screw in place, e) Suturing using 000 black silk suture, f) Postoperative one week following suture removal.

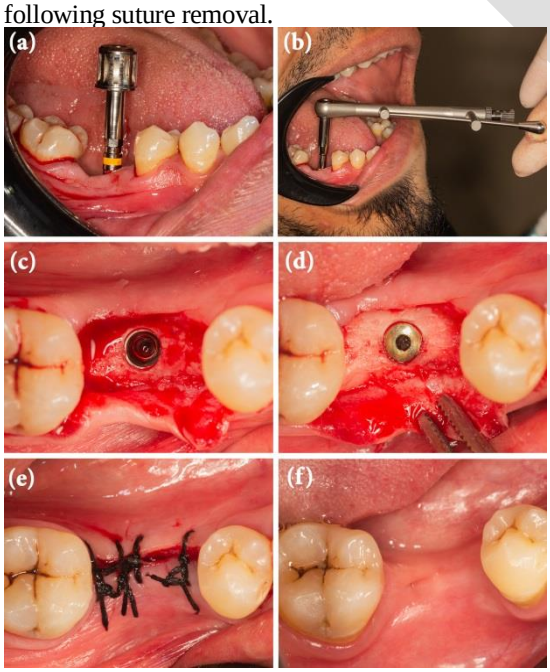

Figure (5): a) Implant insertion using fixture driver, b) Implant screwed into place to the full length using the torque ratchet, c) Implant inserted in the drilled hole, d) cover screw in place, e) Suturing using 000 black silk suture, f) Postoperative one week following suture removal.

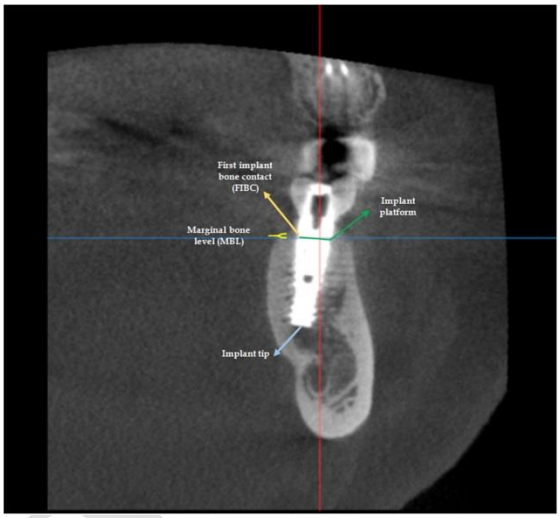

Figure (6): Measurement of marginal bone loss.

Statistical analysis

Data were analyzed utilizing IBM SPSS software package version 20.0**. (**Armonk, NY: IBM Corp**).** Qualitative data were described using percent and number. The normality of distribution was verified using the Shapiro-Wilk test. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). The obtained results's significance was judged at the level of 5%.

The used tests were:

1- Paired t-test

For normally distributed quantitative variables, to compare between two periods**.**

2- Spearman coefficient

To correlate between two distributed abnormally quantitative variables**.**

RESULTS

Fifteen male patients between the age of 30 to 40 years, fulfilling the criteria of inclusion were recruited in this study; none were excluded or lost during follow-up. Their mean age was thirty-five years and were all recruited from the Oral and Maxillofacial Surgery outpatient clinic, Alexandria University. All of the fifteen placed dental implants showed Maximum primary stability immediately after surgical placement, with a mean ISQ (Implant Stability Quotient) = 69, (normal range: 60 – 70) and successful osseo-integration after three and six months of follow up.

No peri-implantitis or lost implants over the 3–6 months' post-implant placement was detected. The minimum bone density preoperatively was 468.20 HU, while the maximum measured bone density was 1888.30 HU. The minimum bone density postoperatively was 467.98 HU, while the maximum measured bone density postoperatively was 1871.91 HU. We found that there was minor reduction in the bone density following the surgical implant placement during the follow up but this

change had no significant difference on the clinical outcome (P = 0.098). **(Table 1)**

In this study, all of the examined patients had normal bone turnover values within the reference range (bone alkaline phosphatase 3.7– 20.9 ng/ml and osteocalcin 2.5–13.0 ng/ml) for men, except for three patients only whose values deviated a little from the normal range. The minimum osteocalcin value was 2.20 ng/ml, while the maximum ostocalcin value was 9.80 ng/ml. The minimum bone alkaline phosphatase value was 3.10 ng/ml, while the maximum bone alkaline phosphatase value was 21.90 ng/ml.

Patients who had abnormal bone turnover values had some reduction in the cancellous bone density compared to their normal counterparts but this reduction was statistically not significant were we have found no correlation between abnormal value of bone turnover markers and reduced bone density. **(Table 2)**

During the follow up phase, the minimum calculated marginal bone loss was 0.07, while the maximum calculated marginal bone loss was 1.17 mm and four patients didn't show any marginal bone loss. **(Table 2)**

There was no significant correlation between marginal bone loss and abnormal bone turnover values with respect to osteocalcin (P = 0.529) and bone alkaline phosphatase (P = 0.613). **(Table 3)**

Table (1): Descriptive analysis of the studied cases according to bone density (n=15)

Bone density (HU)	Preoperative	Postoperative	t	p
Min. – Max.	468.20 – 1888.30	467.98 – 1871.91		
Mean ± SD.	1064.73 ± 434.87	1062.46 ± 433.39	1.72	0.098
Median (IQR)	985.72(802.05–1227.53)	983.74(795.95–1226.74)		

IQR: Inter quartile range SD: Standard deviation

t: Paired t-test

p: p value for comparing between preoperative and postoperative

Table (2): Descriptive analysis of the studied cases according to bone turnover markers and marginal bone loss (n=15)

Bone turnover markers	**Min. – Max.**	**Mean ± SD.**	**Median (IQR)**
Osteocalcin value 2.5–13.0 ng/ml	2.20 – 9.80	5.86 ± 1.96	5.90 (4.85 – 7.0)
Bone alkaline phosphatase value 3.7–20.9 ng/ml	3.10 – 21.90	13.87 ± 4.62	14.10 (11.50–16.05)
Marginal bone loss (mm)	0.0 – 1.17	0.29 ± 0.38	0.13 (0.04 – 0.27)

IQR: Inter quartile range

SD: Standard deviation

Table (3): Correlation between marginal bone loss and bone turnover markers (n=15)

Bone turnover markers	Marginal bone loss (mm)	
	r_s	p
Osteocalcin value 2.5–13.0 ng/ml	-0.177	0.529
Bone alkaline phosphatase value 3.7–20.9 ng/ml	0.142	0.613

r_s: Spearman coefficient

DISCUSSION

Dental implants are one of the highly spectacular modern solutions for replacing lost teeth. The alveolar bone quality and quantity mainly determine the success and longevity of the placed dental implant (31,32). The lack of good bone quantity and quality is considered a risk factor associated with implant complications, including absence of primary stability and defective osseo-integration, that can eventually result in early loss of implant (32).

All of the fifteen placed dental implants showed Maximum primary stability immediately after surgical placement, with a mean ISQ (Implant Stability Quotient) = 69.20 ± 3.01, (normal range: 60 – 70) and successful osseo-integration after three and six months of follow up with no signs of peri-implantitis or lost implants. This could be attributed to following a proper surgical technique while placing dental implants. Our results were consistent with Youssef et al. that recorded a mean ISQ = 67.30 ± 9.14 immediatetly following implant placement (33).

The minimum bone density preoperatively was 468.20 HU, while the maximum measured bone density was 1888.30 HU. The minimum bone density postoperatively was 467.98 HU, while the maximum measured bone density postoperatively was 1871.91 HU and a mean bone density 1062.46 ± 433.39HU. We found that there was minor reduction in the bone density following the surgical implant placement during the follow up but this change had no significant difference on the clinical outcome (P = 0.098), as there was good selection of patients with bone properties that meet successful implant placement. Our results were consistent with Youssef et al. that recorded a mean bone density 1018.0 ± 149.79 HU after six months of follow up (33).

There was minor bone resorption after the implant placement which was figured out -during the follow up. Although it had no significance on the clinical outcome, however it was noticed in most of the cases. This could be attributed to the surgical incision and reflection of the flap is usually accompanied with some degree of bone loss, as a result of the altered vascularization of the bone periosteum after flap elevation. This consequence also occurs following dental implants insertion

which is associated with remodeling processes around the implants, corresponding to some crestal bone loss (34).

During the follow up some patients showed no marginal bone loss while others had minor marginal bone loss with a maximum of 1.17 mm and a mean of 0.29 ± 0.38 mm, after six months follow up. This marginal bone loss could be also related to the implant's surface, design, depth of insertion, platform switching, postsurgical manipulation, the presence of micro-gaps between the abutment and implant and the implant-abutment connection stability, subjected to different forces of occlusion (35). Our results were consistent with Nandal et al. who found the mean bone loss 0.3593 ± 0.37 mm, after six months of follow up following implant placement. (36) The marginal bone loss should not be greater than 1.5 mm in the 1st year (osseointegration period) and 0.1 mm during each successive year (follow-up period) (36). Smith and Zarb suggested that one of the criteria for implant success was that less than 0.2 mm alveolar bone loss is acceptable after the 1st year (37).

The bone is a vital structure that undergoes continuous remodeling and turnover regulated by variety of factors, some are external and others are internal. External factors include diet, exercise, smoking and drug intake which have been all set to standard in this study. While internal factors mainly include the hormonal balance guided by the endocrine system that has both direct and indirect effect on bone formation and resorption. In this study there was minor or no bone loss around the implant during the follow up, and since all the studied subjects were males, the results could be attributed to the influence of male hormones (androgens and testosterone) that stimulate bone growth, in contrast to estrogen; the primary female hormone that inhibit the acquisition bone mineral (34). Moreover, men loose less bone compared to women during the aging process, because they do not run across the physiologic process of menopause (35). Our results were consistent with Yasuda et al. (14).

Also male hormones can have an influence on the value of expressed bone turnover markers. (35)

In this study, all of the examined patients had normal bone turnover values within the reference range (bone alkaline phosphatase 3.7– 20.9 ng/ml and osteocalcin 2.5–13.0 ng/ml) for men, except for three patients only whose values deviated a little from the normal range where this can be attributed to the concept of previously mentioned hormonal balance and role of male hormones in preserving normal ranges of bone turnover values as well as reduced liability for bone resorption.

BTMs play a vital role in the medical field and have begun to show elementary aspect in diagnosis and monitoring various outcomes (38). They are attributes that can be quantified, thus they can reflect the condition of the metabolic process in our body as either normal or pathogenic. Since these biomarkers are highly sensitive and specific, they are able to reflect the biological changes or conditions taking place during any procedure or process. These biomarkers are released into the circulation during the process of bone metabolism indicating the activity of bone remodeling as either osteoclastic resorption or osteoblastic deposition (39). Osteocalcin was commonly expressed during osseo-integration, thereby generally indicating their value in prognostic and clinical performance assessment (40).

Three (20%) of the 15 male patients in this study had a minimum of one BTM value beyond the normal range. There was no or minor marginal bone loss even in the patients who had bone turnover markers' values beyond normal range. Thus there was no significant correlation between marginal bone loss and abnormal bone turnover values with respect to osteocalcin (P = 0.529) and bone alkaline phosphatase (P = 0.613). There was no correlation between abnormal values of bone turnover markers and the presence of marginal bone loss, which could be related to the small sample size that limited the gathered data, the inclusion of few bone turnover markers in the analysis including bone formation markers only as well as analyzing theses markers only preoperatively at baseline with no follow up assessment in the study. (20) Therefore, the levels of BTMs need to be remeasured during the observation phase, as bone turnover is associated with different BTM levels implying loss of bone during the follow-up period (41).

Finally, the realistic aim of BTMs measurement is to assess metabolism of bone in patients already diagnosed with certain bone disease or condition such as osteoporosis; it is not to be used for the purpose of diagnosis (42).

CONCLUSION

From the results of this study we can conclude that:

Surgical interference mostly has an impact on the bone owing to some bone resorption. The chance of metabolic disturbance in men is rarely encountered as majority could have a more organized bone turnover owing to stable normal values of BTMs. There is no correlation between normal or abnormal values of bone turnover markers on the outcome of dental implant treatment, thereby they could not be used to evaluate the bone condition prior to referring to dental implant treatment thus they are not indicators of implant's osseo-integration.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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