

Influence of Vitamin D3 Insufficiency on Dental Implant Success (Randomized Controlled Clinical Study/Original Article)

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Received: June 18, 2020; **Published:** July 15, 2020

Abstract

Purpose: Researcher tried in this article to investigate and emphasize whether vitamin D3 serum levels influences implant success in the early stages of healing.

Material and Method: Clinical study done on 80 patients visiting the private clinic seeking dental implant fixed prosthesis. Patients age where ranged between (20 - 50 years). Patients divided according to Vitamin D3 level into Patients with sufficient level of Vitamin D3 and patients with insufficient level. Sufficiency detected according to Serum 25-hydroxy vitamin D (25-OHD) assay. Each group has 40 participants 100 dental implants. All participants underwent two step traditional dental implant surgeries. Osseointegration evaluated in the second step surgery after 4 months.

Result: Mean age for patients is 37.07; with male to female ratio are 1: 1.58 with no significance relation among groups. Seven dental implant are failure in patients with insufficient level of Vitamin D3 and show significant p value with chi square statistical analysis (.039).

Conclusion: Vitamin D3 insufficiency affect negatively early implant success especially if the vitamin level deficient.

Clinical Relevance: Studies showed that there is a controversial relationship among vitamin D serum levels and osseointegration of dental implants. This relationship is evaluated in animal studies and several case reports. Osseointegration of dental implants depends on bone regeneration; peri-implant bone formation was shown to be reduced in vitamin D deficiency.

Keywords: *Cholecalciferol; Calcium; Postmenopausal Females; Osseointegration; Clinical Study; Bone Healing Process*

Introduction

Missing teeth replacement through endosseous dental implants became a critical part of dentistry. The literature, that in the last two decades, confirmed the success of osseointegrated implants as an applicable replacement for complete and partial edentulous patients [1]. Dental implant surgeries are different with the development of science and technologies. Delayed two steps dental implant procedure is well known for surgeons and dental professionals. Implantation success or failure is related to multiple local or general factors which are most commonly infection and functional load.

Early implant failure is determined as lack of osseointegration for unexplained cause; it can be seen in second step of surgery (gingival former step) [1]. Osseointegration is an idiom expresses the intimate contact between bone and dental implant. In other words, it means the healing process of dental implant in the drilled site. Occasionally, dental implant fails for no reason, when this occurs, it is better to check for any biological abnormalities.

Biological abnormality has seldom been taken as a possible risk factor of early implant failure where loading is not performed yet. One of these important factors is cholecalciferol (Vitamin D3) level, as stated by past studies [2-5].

Vitamin D3 is known as a fat-soluble vitamin which aids the human body to absorb phosphorus and calcium. It is, also, one of the most crucial hormones responsible for the growth of the bones. Moreover, Vitamin D3 reduces the inflammations effects and empowers the immunity reactions of the human body [6].

Vitamin D3 has enormous effect on osteogenesis. The influence of Vitamin D3 on the underlying mechanism and the osseointegration is still uncertain with controversy [7].

According to the physiologically of the bone, the osteoclasts activity is aroused by vitamin D3. Also, vitamin D3 boosts the production of extracellular matrix proteins thru osteoblasts. Moreover, it encourages the absorption of intestinal calcium and restricts the secretion and synthesis of parathyroid hormone. Furthermore, deficiency is connected to healing in patients suffering a fracture and impaired fracture in clinical practice [8].

Insufficiency of Vitamin D3 has been determined as the level of serum which ranges between 21 and 29 µg/l, a serum level below < 20 µg/l as vitamin D deficiency (severe deficiency < 10 µg/l) [9,10].

As to the guidelines of American College of Endocrinology (ACE) and the American Association of Clinical Endocrinologists (AACE), the supplementation is advised to control levels above 30 ng/ml [11]. The society of Endocrine in United States suggest achieving a focus of more than 30 ng/ml of serum 25(OH)D3 and considers the optimal range 40 - 60 ng/ml (Table 1).

Due to the lack of specific guidelines in Iraq, similarly, all hematological laboratories use the (ACE) guidelines, so, researchers use these guidelines for the patients included in the current study.

Early implant failure and vitamin D3 level

Dental Professionals as well maxillofacial surgeons always look for good long-term life osseointegrated dental implant despite of the difficult situations might be occurred in the jawbone.

In dental implantology, vitamin D3 was examined thoroughly as an effective influencing aspect of the bone to implant stability and contact [12].

The connection among vitamin D3, bone metabolism, and early implant failure in human was not confirmed yet clearly. Vitamin D3 evokes the formation of the bone around implants in rodents [12-14]. The formation of peri-implant bone has been reduced in vitamin D3-deficient rats due to the depending of osseointegration of dental implants on the regeneration of bone [15].

Studies showed that there is a controversial relationship among vitamin D3 serum levels and osseointegration of dental implants. This relationship is evaluated in animal studies and several case reports. Majority of research recommend that the healing of peri-implant bone tissue can be enhanced by vitamin D3 adequate serum levels [15].

For such controversy in action of vitamin D3 on early dental implant failure in existed review articles, this article seeks to investigate and emphasize whether vitamin D3 different serum levels has an impact on the implant success in healing at early phases. After four months postoperatively in the second step surgery, un-explained loss in implant osseointegration (implant failure) was seen with no clear cause of failure.

In this article authors consider insufficiency of vitamin D3 serum level less than 29 µg/l and need supplements; while accepted serum level with no need for supplements is above 30 µg/l, serum level (Table 1) [9,10].

Patients and Methods

Ethical approval: All work prepared According to CONSORT 2010 checklist. It's approved by the scientific committee of Nineveh Health Directory/MOH/Iraq by licenses' Number (194) in date (11/3/2019).

More than 200 patients experienced two steps dental implant surgery in the period from (1/1/2015 - 1/1/2018) in private clinic, 80 patients participated in the study. Selection criteria are as follow.

Inclusion criteria

- Patients from 20 - 50 years age at surgery.
- Good oral hygiene.
- Nonsmoker.
- No medical disease history.
- Patient likes to participate.

Exclusion criteria

- Patients with insufficient oral hygiene.
- Bone regenerative therapy before implant placement.
- Medically diseased patients.
- Patients underwent radiotherapy and chemotherapy treatments.
- Pregnant patients.
- Poor follow up patients.

Randomized clinical study was prepared on 80 patients visiting the private clinic seeking dental implant fixed prosthesis. Patient's age was ranged between (20 - 50 years), with no gender specifications. Patients divided into two groups according to vitamin D3 level; each group with 40 participants (100 dental implants). Sufficient level of vitamin D3 (Level above 30 ng/ml) and other group insufficient level of vitamin D3 (Level less than 29 ng/ml).

Each patient has his/her own case sheet with signed ethical approval for participating by him/her after discussing all the steps of surgery.

Dentium Korean Superline System (made in South Korea, Dentium Company) was used for every patient with different numbers of dental implant distributed in each patient individually, at least one dental implant.

All patients were examined generally and locally before surgeries. Intraoral examination includes the site, oral hygiene, soft and hard tissues available, number and diameters of dental implant needed. Periapical and panoramic radiograph used for detection of height and quality of bone available for dental implant. Although CBCT is indicated to be used in the assessment of our patients but as my country is of low economical level, this type of radiograph are available in limited places in the city with high cost and cases operated depends on periapical and panoramic radiographs.

Also, blood samples were collected from all participants to test the cholecalciferol (vitamin D3) serum level for division of patients.

All surgeries were done by the same surgeon under local anesthesia in both placement of dental implant and gingival former step.

Step one surgery

The operation was carried out with the same guidelines for traditional two steps dental implant surgery starting with local anesthesia. Crestal incision was marked on the ridge edentulous part of utilizing Blade Barker No 15. Drilling was carried out in the central part of the alveolar bone. Pilot drill used at first to prepare the socket for the dental implant 2.2 mm, followed by use of final drill based on the implant diameter. Surgical ratchet used for final seating of the dental implant into the bone, lastly the cover screw was seated in place and suturing the flap with 3/0 black silk suture.

Postoperative instructions were explained well One week later, sutures have been removed. Postoperative medications were simple antibiotics use as (Augmentin 1g for 5 days, 1 tablet every 12 hours). All patients were evaluated immediately post-operatively, after two months and in the fourth month post-surgery. Four months were given as healing period before second step surgery took place. Periapical and panorama were taken at the day of second surgery.

Step two surgery

Gingival former step was taken place after four months were healing process almost completed. Under local anesthesia by using tissue punch drill, a small sharp gingival cut was removed over the cover screw which replaced by healing cap or gingival former. At this step, researchers evaluated the dental implant success in both groups, clinical by resonance frequency analysis (RFA) with no pain, tenderness or mobility. Radiographical assessments take place to exclude any bone resorption surrounding implant. Radiographical evaluation by periapical and panorama radiographs examining the bone surrounding the dental implant.

Optimizing vitamin D3 levels

Depending on Serum 25-hydroxy vitamin D (25-OHD) as it considered as a reliable marker of the status of vitamin D3 in many studies; cases distributed. There are no guidelines specified in my country for vitamin D3 level, so the level 30 ng/ml considered regard the test of sufficiency. Less than 29 ng/ml level is considered insufficient and advised to use supplements.

Test group was instructed to take mixture of calcium and cholecalciferol (calcium carbonate 1000 mg + VitD3 0.025 mg) one tablet once daily for three months. One month before surgery and two month after surgery.

Table 1 is a descriptive scale for all concentrations and vitamin D levels in human. The authors consider level below 29 ng/ml defines as insufficiency and 30 ng/ml; above that level define as sufficiency [11].

Status	Serum 25 OH	Vitamin D Concentration
Severe Deficiency	< 10 ng/ml	< 25 nmol/liter
Deficiency	< 20 ng/ml	< 50 nmol/l
Insufficiency	21 - 29 ng/ml	50 - 74 nmol/l
Sufficiency	30 - 100 ng/ml	75 - 250 nmol/l
Optimal	30 - 60 ng/ml	75 - 150 nmol/l
Toxic	> 150 ng/ml	> 375 nmol/l
Pre-surgery	40 - 60 ng/ml	100 - 150 nml/l

Table 1: Vitamin D concentrations and level in humans (Pludowski P, et al. 2018).

Statistical analysis

Statistical Package for Social Sciences (SPSS) software program IBM version 20, Chi-Square Tests was used to analyze data for mean, percentage and significance.

Result

Eighty participants (80) were included in the study. The participants were divided into two groups depending on vitamin D level.

Table 2 shows descriptive statistic where mean age for patients is 37.07, with mean dental implant number in each patient is 2.5. The third decade age group are forming the most common age group underwent implant surgery (Figure 1) with 45 patients.

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
Age	80	23.00	45.00	37.0750	5.59786
Dental implant	200	1.00	7.00	2.5500	1.33027
Failure	200	.00	2.00	.0875	.32584

Table 2: Descriptive statistic of the sample.

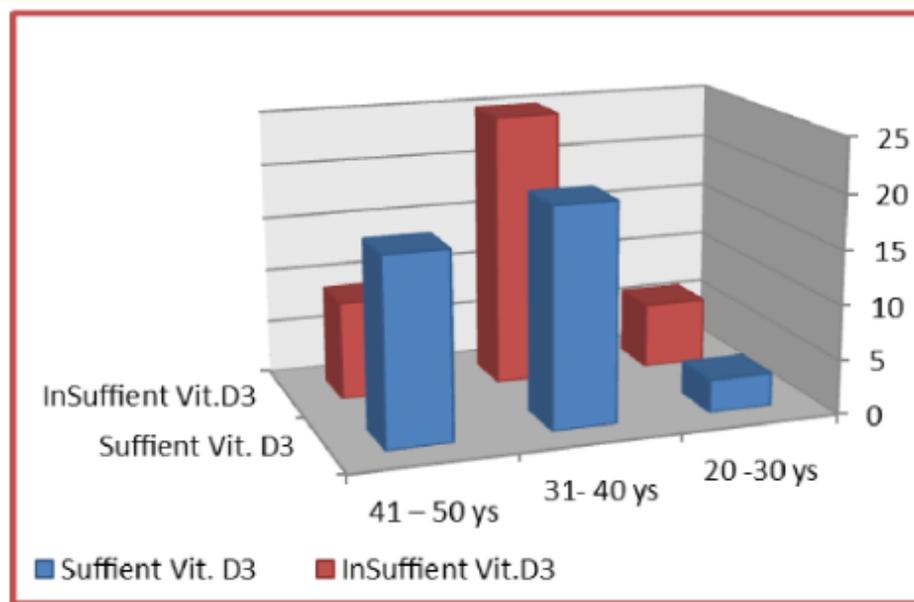


Figure 1: Age distribution among groups.

Females formed the high incidence with male to female ratio are 1: 1.58 were female count 49 patients (Figure 2).

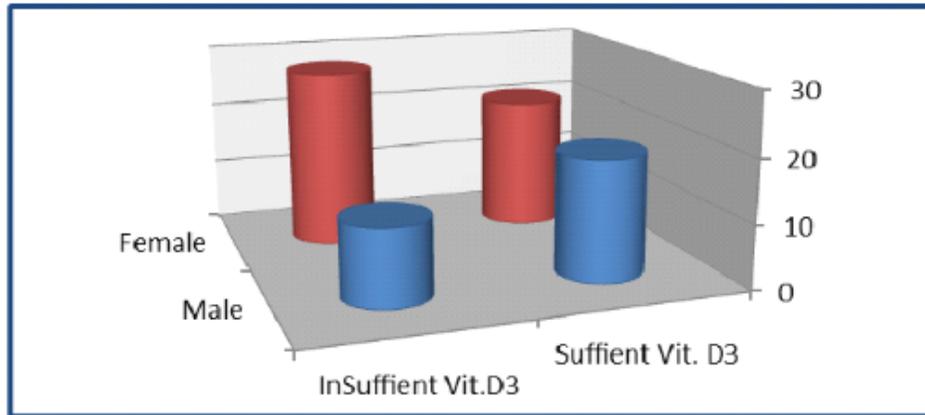


Figure 2: Gender distribution among groups.

Seven dental implants are failed from total 200 implants, at the time of second step surgery in patients with insufficient level of Vitamin D3. Figure 3 expresses dental implant failure rate among groups in relation to Vitamin D3 Level.

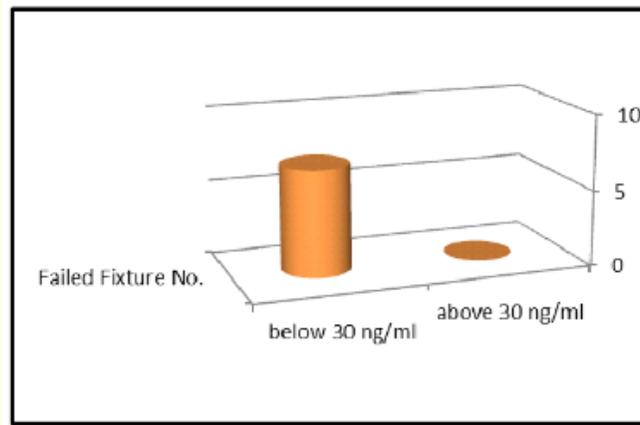


Figure 3: Vitamin D3 level failure.

Analyzing vitamin D3 level with age, gender and failure rate is done. Chi-Square Tests show no significant relation between vitamin D3 and age group. Likewise, there was no significant relation between vitamin D3 level and gender (respectively 0.629, 0.108). While significant p value (.039) observed in patients with insufficient level of Vitamin D3. Table 3 show Vitamin D3 Level Comparison with age, gender and failure.

Comparison Items	Pearson Chi-Square		
	Value	Df	Asymptotic Significance (2-sided)
Age	17.362	20	.629
Gender	2.581	1	.108
Failure	6.486	2	.039

Table 3: Vitamin D3 level comparison with age, gender, failure.
P value is less than 0.05. Normal Significant.*
N of Valid Cases = 80.

Discussion

Maxillofacial surgeons and Dental professionals are always seeking for high success criteria in implant hating failures.

Mihoko., *et al.* considered osseointegration as a secondary stability for the dental implant inside the bone bed and it is depending on conditions of surrounding tissues. Therefore, it has been considered as utmost important to quantify implant stability at various times. Additionally, radiographs can be an available method to evaluate the stability of pre and postoperatively [16].

Cholecalciferol is synthesized in the skin naturally when it is exposed to sunlight; also it can found in many foods and patient can take it as it as a dietary supplement [17].

Serum 25 OH vitamin D3 level test is the most popular guides used all over the wards and the specific level for difference between sufficient and in sufficient is above or below 30 ng/ml, for that reason we follow this guidelines as a point of division of cases [18-20].

Alves., *et al.* highlight vitamin D bone mineralization importance, and also focus on that insufficiency is able to increase the possibilities of some sickness of including diseases of bones [21].

Supplementation of vitamin D gives a positive influence among patients of vitamin D-deficient. However, research on the influence of supplementation on bone healing and deficiency of vitamin D are scarce and still need further investigation [22].

Deficiency of Vitamin D has a huge effect on mechanisms of bone healing, and majority of studies affirmed the critical role of vitamin D in density of bone mineral and the necessity to keep adequate levels of vitamin D in the body [23-26].

Cholecalciferol insufficiency is caused by many reasons, the most important one that they don't absorb the suggested levels of the vitamin if it is exposed to sunlight or over time.

Articles shows that deficiency vitamin D is recognised as a worldwide health issue and is to be to be increased in the future due to the changes of demographic which reflect an aging population [27].

On the basis of this perspective, researchers have the idea to emphasize the effect of insufficient vitamin D3 in the selected patients who sustain dental implant surgery. Furthermore, in the last years, my city (Mosul/Nineveh) had a very difficult situation that affected nutrition and food dietary supplements because of ISIS war and low or even no sun exposure as all people hide in their basement floor in addition very poor daily feeding supplement because of ISIS blocked. Make patients present with poor health. In addition, surgeons

experienced unreasonable failure of dental implant at the early time, however, lack of osseointegration in this manner which was un-experienced before.

Epidemiological research demonstrates that roughly 70% of population is deficient [28]. Similarly, my city was affected by this theory, besides that, we pass in situations of embargo affect the families economically can result in this deficiency.

Early dental implant failure (EDIF) defined as the lack of osseointegration which should occur within 4 months after placement, before the connection of the prosthetic abutment where the dental implant still un-functioning [20]. Until recently, only a few studies have investigated the possible connection between serum levels of vitamin D and EDIF.

In age selection criteria, researcher tried to exclude the patients who are older than 50 where the age of bone disease might affect or add another reason rather than vitamin deficiency as post menopause causes. Good response to dietary and drug supplements which were advised for patients prove the results showed as age and gender have no significance result in relation to vitamin D3.

Engy, *et al.* described the effect of cholecalciferol in postmenopausal, only females were chosen whose age group ranged between (40 - 60 years). The study concluded that enhancement for good success in dental implants even in such situations. The results showed an increase in bone density [1,20].

Calculation of drugs supplements followed the popular guidelines described by physicians similar to the level of detections guidelines which try to avoid side effects of the extra use supplements that can alter the results of the study [29,30]. The doses of vitamin D3 are given by physician.

In line with previous studies, this study can accomplish that there is a significant (.039) relationship between the level vitamin D3 and early failure in dental implants. Unfortunately, in spite of using of supplements, seven dental implants were also lost, that might be related to deficiency of vitamin D3, and not only insufficiency. That means the level is below 20 ng/ml and the supplement not enough to regulate that level. This impression was proved when we go back to our patients to check again for what we think we need other guidelines that conflict the society in the country.

Freitas clarified that vitamin-D deficiency may lead to harsh diseases, like bone atypical mineralization, as it lessens the barriers activity, so he clinched that vitamin D effects the cellular operation of bone curing and that the exact technique of this effect still not obvious [31].

Fischer V also point out on that vitamin D and calcium are critical for maintaining the health of the bone although the mechanism is still unclear [32].

In addition, Choukroun J agreed with Kelly J [5,8] that osseointegration of dental implants relies on the regeneration of the bone, the formation of peri-implant bone was decreased in vitamin D-deficient rats. Astonishingly, few preclinical results of vitamin D supplementation effect on the regeneration of bone are available.

According to association of dental Implantology (ADI) success means that implant is present at the time of examination and fulfills certain pre-established criteria such as no pain, radiolucency, no bone loss, no peri-implant pocketing [33].

Richard J Miron highlighted the fact that, lately, new studies have shown a significant and noticeable increase in early failure of dental implants which around 300% higher than standard healthy implants. Moreover, debate about a recovery program and supplementation were discussed as ways to help patients in the healing both pre-surgically and in the recovery of patients representing low levels of vitamin D [14].

Miron also paid attraction to the past studies of initial pre-clinical research showing the enormous vitamin D deficiency impact on osseointegration. Other clinical researches were shown this began initially as case reports [14].

Choukroun J in 2014 noted that implant osseointegration failure result from infection observed in low vitamin D deficiency so that he proves that deficiency may be a risk factor for early failure [8].

In study done by Fretwurst they proved that after a six months' time of healing and the supplementation levels of vitamin D were increased ($> 46 \mu\text{g/l}$), and implants have been successfully osseointegrated in every cases after adequate supplement [6,34]. Researchers suggested that future randomized clinical trials could be used to examine the connection among implant failure and vitamin D deficiency.

Insua dedicate extensively on insufficiency effect of vitamin D3 and early implant failure prove the importance of such missed factor [35].

To date, the widest research on implant failure rates are conducted by Mangano where around 2000 implants have been studied in nearly 1000 exciting, deficiency of vitamin D severe (defined as serum levels $< 10 \text{ ng/mL}$) was showed at nearly a 300% increase in the total implant failure rates when comparing to controls [20].

Miron emphasized that it's essential to supplement patients before implant surgery upon detection of low patient vitamin D levels. At least four weeks supplementation program was suggested before the surgery followed by two weeks post-op [14].

Cholecalciferol level can be considered as hidden risk factor for individuals with no obvious complain might end with early dental implant loss. Supplement use can improve level of implant osseointegration as only seven implants were failed from 100 implants seated in patients with insufficient vitamin D3.

Limitation of the Study

Some limitations in this study attributed, it should be explained for the researchers. One of these limitations that concerning detection of the secondary stability radiograph, it's better to use cone beam CT scan which gives more accurate detection. Second limitation, the researchers believe that larger sample size could give more authentic and general results i.e. research data in excesses of 200 dental implants.

Conclusion

Despite limitations, the study approve that role of vitamin D status in patients underwent dental implant surgery need to be keep in mind in patients assessment as it can negatively affect the healing process of dental implant. Dental implants durability might need to set new guidelines to better control. It is author's estimation that periodic assessments of vitamin D3 with new guidelines for level estimation according to population are mandatory.

Acknowledgements

- We appreciate the role of Scientific Committee of Nineveh Health Directory for their help in approving the research ethically.
- Great thankful for the Assistance Staff they perform smooth surgeries.

Funding Sources

No Funding Sources.

Conflict of Interest

Authors have no conflict of interest.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Author Contributions

Author is contributed to acquisition, statistical analysis and interpretation of data, drafted the manuscript and critically revised the manuscript for important intellectual content.

Author gave final approval and agrees to be accountable for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Volume 19 Issue 8 August 2020

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