

# The Relationship Between Serum Level of Vitamin D3 and Osseointegration Around the Dental Implant

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At present, dental implants are used more than before, and their high success rate is attributed to sufficient osseointegration, which depends on prosthetic-, implant-, and patient-related factors. The quality and quantity of bone and the host response are the main patient-related factors. Vitamin D3 affects bone metabolism by stimulating both osteoclasts and osteoblasts. This study aimed to review the human studies on the efficacy of vitamin D3 for dental implant osseointegration. Search of the literature yielded only 4 studies on human models, of which 2 showed the optimal efficacy of vitamin D3 for dental implant osseointegration, whereas the remaining 2 did not report any positive effect. However, this finding may be related to the small sample size of the vitamin D3-deficient group, which can compromise statistical analyses. In conclusion, vitamin D3 seems to be effective for dental implant osseointegration, although further research is required on human models.

**Key Words:** vitamin D3, deficiency, osseointegration, dental implants

## INTRODUCTION

Dental implants are a successful treatment modality for restoring both function and aesthetics.<sup>1,2</sup> Dental implant treatment has predictive results in replacement of the lost teeth and has a high success rate even in the long term.<sup>3,4</sup> The osseointegration of dental implants plays a fundamental role in their long-term survival. Optimal osseointegration requires a direct contact between the bone and implant surface, without any intervening fibrotic tissue.<sup>5</sup> Dental implants should be osseointegrated during the primary healing phase to firmly yield fixed implants with no clinical signs or symptoms under functional loads. This integration should be preserved over time.<sup>1,6</sup> The osseointegration of dental implants depends on surgical and prosthetic factors such as the technique of surgery,<sup>3,7</sup> time passed since implant placement, and type of prosthetic loading.<sup>8</sup> In addition, it depends on implant-related factors such as the implant material, design,<sup>9</sup> and surface topography,<sup>10</sup> and patient-related factors including the quality and quantity of the host bone and the host response.<sup>3,6,11</sup>

During recent years, many studies have focused on surgical and prosthetic factors, as well as the implant-related factors.<sup>9,10</sup> However, implant failure still occurs despite the improvements that have led to increased survival rate of dental implants,<sup>12</sup> which suggests the possible role of some host-related risk factors.<sup>13</sup>

Vitamin D3 is a fat-soluble vitamin, acquired through the diet or synthesis in the skin after exposure to ultraviolet light.<sup>14</sup> The inactive form of vitamin D3 converts to the active form (ie,

1,25 dihydroxyvitamin D3 in the liver and kidneys).<sup>15,16</sup> Vitamin D3 deficiency can adversely affect the brain,<sup>17</sup> respiratory tract,<sup>18</sup> cardiovascular system,<sup>19</sup> skin, immune system, and endocrine system.<sup>20</sup> In addition, vitamin D3 plays a pivotal role in bone metabolism by stimulating osteoclasts and increasing the production of extracellular matrix protein by osteoblasts.<sup>21</sup> Measuring the serum level of 1,25 dihydroxyvitamin D3 is currently the most appropriate way to assess the serum level of vitamin D3. The serum levels of vitamin D3 < 10 ng/mL represent deficiency, levels between 10 and 30 ng/mL indicate insufficiency, and levels > 30 ng/mL are considered normal.<sup>15,22</sup>

Considering all these factors, the efficacy of vitamin D3 for enhancement of dental implant osseointegration is not yet clear. Therefore, the present study aimed to review the available human studies on the effect of vitamin D3 deficiency on dental implant osseointegration.

## MATERIALS AND METHODS

An electronic search was carried out in the Web of Science, Scopus, Ovid, Embase, PubMed, and Google Scholar databases for articles published until October 10, 2019 using the keywords "implant," "dental implant failure," "dental implant," "vitamin D3," and "vitamin D3 deficiency." The search was limited to English articles on human models, and review articles, in vitro experimental studies, and animal studies were excluded. Data regarding the study design, sample size, sex, and age of patients and number of implants were extracted and recorded in a checklist.

## Results

Only 4 studies met the eligibility criteria (2 case reports and 2 retrospective studies), which were reviewed, and the following results were obtained.

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Surg et al reported a 29-year-old patient (they did not report the sex of the patient), who received 1 implant in the right first premolar region of the mandible (Nobel Replace RP 4.3\*10). Five months after implant placement, the patient was recalled for the second-stage surgery. No inflamed tissue was observed when elevating the flap; however, the implant was mobile. Thus, they removed it. At the time, the serum level of vitamin D3 of the patient was <10 nmol/L.

Tobias et al discussed 2 patients in their case report. The first patient was a 48-year-old man who had received 2 implants (Straumann) in the mandibular left first and second molar regions. The next day, the patient complained of pain; no osteolysis around the implants was observed on the radiograph. Both implants were removed after 3 days of constant severe pain. Extensive osteolysis was observed during the surgical extraction of implants. After 6 months, 2 implants (Straumann) were placed again in the same region. At the time, the mandible seemed to be well vascularized, without any granulation tissue. Again, both implants were removed after 3 days because of constant severe pain without any sign of soft tissue inflammation or abscess formation. In the next step, the vitamin D3 level of the patient was measured, which was found to be 11 µg/L. After 6 months of taking vitamin D3 supplements, the third surgery was performed to place 1 implant (Conelog Screwline) in the first molar region. The vitamin D3 level was 46 µg/L. Finally, the surgery was successful, and prosthetic treatment was subsequently performed as planned. The second patient was a 51-year-old man who received 2 implants (Straumann) in the mandibular left first and second molar regions. One day after surgery, the patient reported a sense of discomfort at the surgical site. At 7 days postoperatively, the patient complained of severe escalating pain. Pharmaceutical therapy with 600 mg ibuprofen was not effective, and the implants were removed at 15 days postoperatively. The serum level of vitamin D3 was 20 µg/L. After 4 months of vitamin D supplementation, 1 implant was placed in the second molar region. In the follow-up session, no problem was observed, and prosthetic treatment was performed as planned.

Francesco et al conducted a retrospective study on 1740 implants placed in 885 patients, including 455 males and 430 females. The mean serum level of vitamin D3 was 29.5 ng/mL in patients. The incidence of early failure in patients with an acceptable level of vitamin D3 (>30 ng/mL) was found to be 2.9%. However, this rate was almost double (4.4%) for individuals with insufficient levels of vitamin D3 (10–30 ng/mL). The incidence of early failure was almost 4 times higher (around 11.1%) in patients with severe vitamin D3 deficiency (<10 ng/mL). The  $\chi^2$  test did not reveal any significant difference ( $P = .105$ ), although a clear association was noted between higher incidence of early dental implant failure and serum vitamin D3 deficiency.

Francesco et al<sup>26</sup> performed a retrospective study on 1625 implants in 822 patients (424 males and 398 females). The mean serum level of vitamin D3 was 29.9 ng/mL in patients. The incidence of early dental implant failure in patients with vitamin D3 level > 30 ng/mL was 2.2%, whereas the incidence of early dental implant failure in individuals with insufficient vitamin D3 level (10–30 ng/mL)

was twice the rate in the first group (3.9%). This rate was 9% in those with vitamin D3 deficiency (<10 ng/mL). Statistical analysis indicated no significant difference, although the incidence of failure was higher in those with vitamin D3 deficiency ( $P = .15$ ).

## DISCUSSION

Studies on the relationship of serum level of vitamin D3 and dental implant osseointegration are limited; most of the available studies on this topic have been conducted on animal models, and only a few of them are human studies. Javed et al,<sup>27</sup> in their systematic review, evaluated 6 animal studies (4 on rodents and 2 on rabbits), of which 5 reported increased bone-to-implant contact (BIC) around dental implants after vitamin D3 supplementation. Although no significant difference was found between dental implants coated with vitamin D3 and regular implants in a study on BIC, the results indicated that both types of coated and noncoated implants had a rough surface, and the effect of vitamin D3 deficiency probably decreased because of compensation by surface roughness of implants, because surface roughness can promote osseointegration.<sup>28</sup> In another study, James et al evaluated rats and found that vitamin D3 deficiency significantly impaired dental implant osseointegration. Jacob et al reported that less bone matrix was formed around the implants 3 weeks after implant surgery in rats with vitamin D3 deficiency. In addition, Choukroun et al,<sup>31</sup> in their literature review, reported that vitamin D3 is essential for linking innate and acquired immunity. Thus, vitamin D3 deficiency can increase the risk of infection and compromise implant osseointegration. However, Akhavan et al<sup>32</sup> indicated that vitamin D3 did not affect dental implant osseointegration. Their contradictory results could be attributed to the inadequacy of the dosage and duration of administration of vitamin D3.<sup>32</sup>

In the present study, 2 of the reviewed studies indicated the effect of vitamin D3 deficiency on the BIC,<sup>23,24</sup> whereas no statistically significant difference was observed in early dental implant failure between patients with sufficient vitamin D3 and those with vitamin D3 deficiency in 2 other studies.<sup>25,26</sup> In the latter 2 studies, a greater tendency to fail was evident among the individuals with vitamin D3 deficiency. However, the number of individuals with vitamin D3 deficiency in both studies was very low, and this small sample size can compromise the accuracy of the comparison between the study groups and may explain insignificant results.

## CONCLUSION

Based on the current results, it seems that vitamin D3 may play a significant role in enhancing the BIC and bone volume around dental implants. To date, randomized clinical trials and prospective studies on this topic have not been conducted on human models. Therefore, further studies with precise statistical analyses are required to further scrutinize the relationship of diminished serum level of vitamin D3 with reduction of BIC and increased implant failure rate.

## ABBREVIATION

BIC: bone-to-implant contact

## NOTE

The authors declare no conflicts of interest.

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