ORIGINAL ARTICLE

# Examining the effect of serum level of Vitamin D on union of tibia closed fractures

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## Abstract

**Introduction:** Impaired fracture healing process may lead to prolonged disability, anxiety, and psychological burden on patients, as well as the imposition of additional costs on the treatment system and the patients. The roles of Vitamin D in fracture union process have not yet been clearly determined. Therefore, the present study was aimed to examine the effect of serum level of Vitamin D on the union of tibia-closed fractures. **Method:** This was a prospective clinical trial conducted on 46 patients with closed tibial fractures. Serum levels of Vitamin D were measured and recorded before surgery using blood tests in all patients. The union process was evaluated through clinical and radiographic evaluations on a weekly basis up to 4 weeks after surgery and then monthly. The patients were divided into two union groups before 6 months of fracture and the group with union disorder after 6 months and presurgical values of Vitamin D were compared between two groups. $P < 0.05$ was considered as statistical significance for all tests. **Results:** Mean level of Vitamin D in the union group before 6 months (19.6 ± 13.6) was higher than the group with union disorder (15.3 ± 7.4), it was not significantly different ($P = 0.147$). Pearson correlation coefficient showed an inverse relationship between the Vitamin D levels with the time of union, so that with increasing levels of Vitamin D, the duration of union reduced, but their relationship was not statistically significant ($P > 0.05$). **Conclusion:** There was no significant correlation between serum Vitamin D levels and the union of the tibia fracture, and given the contradictory results in previous studies and the prevalence of Vitamin D deficiency in Iran, studies with more samples are recommended.

**Key words:** Tibia fracture, union, Vitamin D

## INTRODUCTION

Fracture healing is a unique, complex, and continuous physiological process consisting of five overlapping processes including hematoma, inflammation, soft bone formation, hard bone formation, and bone re-formation stage,[1-3] Fracture union disorder may be caused by different factors including poor nutritional status, which results in prolonged disability and, in some cases, significant pain.[1,3] Different studies have demonstrated that nutrition plays an important role in fracture healing process, but it has not been considered as a predicting marker along with the conventional clinical and radiographic diagnosis.[3,4] Vitamin D is also a key factor in the fracture healing process.

The findings of studies on Vitamin D deficiency or its complementary effect on fracture repair were unclear, contradictory, or controversial in human studies, in contrast to animal studies.[5-8] The findings of a study showed a positive effect of supplementing Vitamin D3 and calcium on bone repair in older women with bone loss and bone fracture.[9,10] Although the results have showed no significant correlation between Vitamin D deficiency and occurrence of delayed or non-union of bones,[11] several studies demonstrated that the Vitamin D insufficiency may be associated with occur kinds of fractures especially in elderly patients. Therefore, the serum level of Vitamin D may be a useful index for the risk of fractures in elderly patients.[12]

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Disorder in the repair of tibia fractures is a common challenge for surgeons. As the exact role of Vitamin D in helping to improve tibia fractures has not been shown yet, the study was designed to examine the effect of serum levels of Vitamin D on the union of fractures.

## MATERIALS AND METHODS

This study was designed as a prospective clinical trial and conducted on the patients with closed tibial fractures ($n = 46$) who were the candidate of surgical nail fixation admitted to Imam Khomeini and Golestan Hospital, Ahvaz, Iran.

Serum levels of Vitamin D of all patients were measured and recorded before surgery. Vitamin D as D ≥30 ng/ml was considered normal and D <30 ng/ml as abnormal. After discharge from the hospital, fracture union evaluation was performed using clinical-radiographic assessments (anterior and lateral examination) weekly up to 4 weeks after surgery and then monthly. The union was measured with the radiographic union score for tibial (RUST), where RUST scores ≥7 are acceptable. The RUST score, some scores were assigned to all four cortices (the fracture line without the formation of callus = 1; callus and the fracture line = 2; and callus without a fracture line = 3), and their sum was considered the final score. The fracture union time was recorded for each patient. All of the experiments of this study were approved by local Ethics Committee in Ahvaz Jundishapur University of Medical Sciences (AJUMS), Ahvaz, Iran (IR.AJUMS.REC.1395.328), which were in complete agreement with the instructions for human studies in Helsinki treaty (2014). After explaining of the study procedure and potential and risk of experiments to the candidates, the informed consent form was obtained from all patients. Inclusion criteria of the study were the patients with closed tibia fracture and nail fixation surgery. The exclusion criteria were an open fracture, history of fractures in the limbs, smokers, alcoholics, long-term users of anabolic steroid drugs, patients with osteoporosis, and metabolic diseases and diabetes. During the study, 23 patients were excluded from the study for different reasons including mortality, migration and inaccessibility, rebound fracture, lack of referral after opening splint, and the impairment diagnosis in laboratory response. Finally, the results of 46 patients were collected, and data were analyzed with statistical package SPSS (Windows, version 22) using a *t*-test, Chi-square, Pearson correlation, and regression tests. The quantitative variables are represented as the mean ± standard deviation (SD).

**Table 1:** Demographic information of patients

| Variables | Union (%) | Nonunion (%) | *P* |
|---|---|---|---|
| Gender | | | |
| Men | 26 (89.7) | 14 (82.4) | 0.478 |
| Women | 3 (10.3) | 3 (17.6) | |
| Age (year) | 27.7±7.8 | 31.3±10.7 | 0.199 |

*The difference is significant at the 0.05 level

**Table 2:** The results of a study of Vitamin D levels in all patients

| Variables | Union (%) | Nonunion (%) | *P* |
|---|---|---|---|
| Vitamin D | | | |
| <30 | 18 (75) | 14 (93.3) | 0.147 |
| ≥30 | 6 (25) | 1 (6.7) | |

*The difference is significant at the 0.05 level

## RESULTS

A total of 46 patients with a mean age of 29 ± 9.1 (SD) years completed the study and were divided into two groups according to the duration of treatment: Complete union in 6 months (union) ($n = 29$) and patients unacceptable (nonunion) fracture union 6 months after ($n = 17$). There were no significant differences between the two groups regarding the distribution of gender and age [Table 1].

There was no significant difference between the levels of Vitamin D in both groups [Table 2].

The level of Vitamin D in patients with bone union within <6 months was examined separately according to the union time in the month. There was no significant difference between Vitamin D levels [Table 3].

The relationship between Vitamin D level and fracture time was calculated using the Pearson correlation coefficient [Table 4].

The results of Pearson correlation coefficient showed an inverse relationship between the level of Vitamin D with union time, meaning that the increase in the level of Vitamin D decreased during union time, but their relationship was not statistically significant ($P > 0.05$).

**Table 3:** Comparison of Vitamin D levels in patients with union <6 months separately by union time

| Variables | Time of union (%) | | | | *P* |
|---|---|---|---|---|---|
| | 3 months | 4 months | 5 months | 6 months | |
| Vitamin D | | | | | |
| <30 | 4 (22) | 8 (44) | 5 (28) | 1 (6) | 0.865 |
| ≥30 | 2 (33.3) | 2 (33.3) | 2 (33.3) | 0 (0) | |

**Table 4:** Correlation matrix of the relationship between Vitamin D and union time

| Variables | Mean±SD | Correlation |
|---|---|---|
| Vitamin D | 22.3±15.8 | −0.132 |
| Union time | 4.14±0.83 | |

**Table 5:** Predicting union time based on Vitamin D in patients with union <6 months

| Criterion variable | Predictor variable | *R* | $R^2$ | ANOVA | | Coefficients | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | F | *Pe* | B | SEB | B | T | *P* |
| Time of union | | 0.193 | 0.037 | 0.408 | 0.67 | | | | | |
| | Constant | | | | | 5.55 | 1.9 | | 2.86 | 0.009 |
| | Vitamin D | | | | | −0.01 | 0.012 | −0.177 | 0.788 | 0.44 |

In addition, simultaneous regression analysis was used for examining the ability of the means of the level of Vitamin D in predicting the time of the union of <6 months [Table 5].

According to the results of Table 5, Vitamin D explain 3.7% of the total union variance in patients with <6 months of the union ($R^2 = 0.037$). One-way analysis of variance did not report prediction of union time by Vitamin D as significant (F = 0.408 and $P = 0.670$). Considering the reported coefficients of prediction of union time prediction, Vitamin D has not been able to predict union time in patients significantly.

## DISCUSSION

The study evaluated the effect of serum levels of Vitamin D on the union of tibia fractures, so that if we found a positive correlation between serum levels of Vitamin D with the time of the union of tibia fractures, pay more attention to the serum levels of Vitamin D in these patients. Moreover, this should be included in laboratory routine tests and targeted as a therapeutic marker and given nutritional recommendation and supplements shorten the time of union.[5,12,13]

Although our study showed no significant differences in the Vitamin D levels between the patients with the union before 6 months and the patients with nonunion, the number of patients with Vitamin D deficiency in the nonunion group was greater than another group. Brinker *et al*. reported that 68% of the nonunion patients showed Vitamin D deficiency of them 57% had 25 hydroxy Vitamin D (25 OHD) metabolite.[14] These findings support our finding on the difference of Vitamin D level between nonunion group and the union group.

There was a reverse relationship between the mean levels of Vitamin D with mean union time in patients with union <6 months, so that the increase in Vitamin D levels decreased union duration, but this relationship was not statistically significant. In the present study, Vitamin D failed to predict union time in patients significantly.

Similarly, Vitamin D levels in the study by Tauber *et al*. were significantly lower in the nonunion group.[15] In the study by Haining *et al*., there were no significant differences between serum nonunion patient and union patients.[16] In a systematic review study, Gorter *et al*. showed that although the role of Vitamin D was effective in fracture repair, the findings of various studies on the significance of this relationship were contradictory.[9]

## CONCLUSION

The results of the study showed no significant correlations between serum Vitamin D levels and the union of the tibia fracture, and according to the contradictory results in previous studies and the prevalence of Vitamin D deficiency in Iran, some studies with more samples are suggested.

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