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Role of Serum Vitamin D and Calcium Levels in Fracture Healing and Functional Recovery: A Clinical Correlation Study

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ABSTRACT

Background: Fracture healing is a complex physiological process influenced by multiple biological and nutritional factors. Vitamin D and calcium are essential for bone mineralization and remodeling, yet their deficiencies are highly prevalent in developing populations and may adversely affect healing outcomes.

Objective: To evaluate the role of serum vitamin D and calcium levels in fracture healing and functional recovery among adult patients.

Methods: This prospective observational study was conducted at the Department of Orthopaedics, Nishtar Medical University, Multan, Pakistan, from January 2022 to January 2025. A total of 160 adult patients with acute long bone fractures were included in the study. Baseline serum 25-hydroxyvitamin D [25(OH)D] and calcium levels were measured at the time of enrollment. Patients were followed for up to 12 weeks to assess radiological union and functional recovery using standardized scoring systems. Statistical analysis was performed using SPSS version 26.0.

Results: Vitamin D deficiency was observed in 57.5% of patients, while hypocalcemia was present in 35.0%. Patients with sufficient vitamin D levels showed significantly faster fracture healing (9.1 ± 1.7 weeks) compared to deficient patients (11.9 ± 2.5 weeks, $p < 0.001$). Similarly, normal calcium levels were associated with shorter healing time (9.8 ± 1.9 weeks) compared to hypocalcemia (11.5 ± 2.4 weeks, $p = 0.002$). Functional recovery scores were significantly higher in patients with adequate vitamin D and calcium levels. Multivariate analysis identified vitamin D deficiency and hypocalcemia as independent predictors of delayed healing.

Conclusion: Serum vitamin D and calcium levels significantly influence fracture healing and functional recovery. Early identification and correction of deficiencies may improve clinical outcomes.

Keywords: Vitamin D, Calcium, Fracture Healing, Functional Recovery, Bone Health.

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INTRODUCTION

Fracture healing is a complex biological process involving a sequence of inflammatory, reparative, and remodeling phases that collectively restore the structural and functional integrity of bone [1]. This process is regulated by a multifactorial interplay of cellular activity, mechanical stability, vascular supply, and biochemical factors.

The micronutrients, including vitamin D and calcium, are especially important in bone regeneration and mineralization and are thus key factors in the successful fracture healing and functional recovery [2].In its active form (1, 25- dihydroxyvitamin D), vitamin D plays a significant role in the regulation of calcium homeostasis by increasing intestinal calcium absorption and regulating bone turnover [3].

It stimulates the development of osteoblasts and mineral deposition of the fracture callus, which is directly involved in bone formation. Calcium, however, is an essential constituent of hydroxyapatite crystals, which furnish mechanical strength to newly-formed bone. In

fracture healing, metabolic requirement of calcium increases tremendously, as it is important in the maturation and mineralization of callus [4].

Although vitamin D has clearly defined physiological roles, its deficiency has become an epidemic issue among the population, especially in developing nations like Pakistan [5]. The causes and contributing factors to hypovitaminosis D include: the lack of sunshine exposure, deficiency in the consumption of food, lifestyle trends in towns and the cultural aspects. Likewise, the lack of calcium is not a rare case, and can impair the skeletal health even more. These shortcomings are especially critical when it comes to fracture management where the optimal nutrition status is needed to ensure the timely and effective repair of the bones [6].

New clinical data indicates that low levels of serum vitamin D are linked to slow fracture healing, risk of non-union and worse functional outcomes. Hypocalcemia can also negatively affect the mineralization stage of bone healing, leading to callus formation that is weaker and an extended recovery. However, the existing literature remains inconclusive, with some studies reporting minimal or no direct effect of supplementation on fracture union rates, thereby emphasizing the need for further clinical correlation studies [7,8].

In addition to radiological union, functional recovery has become an increasingly important outcome measure in orthopedic research, reflecting a patient's ability to resume daily activities and maintain quality of life. The relationship between micronutrient status and functional outcomes has not been extensively investigated, particularly in resource-limited settings [9].

Given the high prevalence of vitamin D and calcium deficiencies and the lack of consistent clinical evidence, the present study aims to evaluate the role of serum vitamin D and calcium levels in fracture healing and functional recovery. The study seeks to provide clinically relevant evidence to support routine biochemical assessment and targeted nutritional interventions in fracture management through a clinical correlation approach [10].

MATERIALS AND METHODS

This prospective observational clinical correlation study was conducted in the Department of Orthopaedics, Nishtar Medical University, Multan, Pakistan, over a three-year period from January 2022 to January 2025. The study was designed to evaluate the association between serum vitamin D and calcium levels and fracture healing as well as functional recovery in adult patients with acute fractures. A prospective design was adopted to allow sequential assessment of biochemical parameters alongside clinical and radiological evaluation of healing over a defined follow-up period.

A total of 160 adult patients were enrolled using a non-probability consecutive sampling technique. Eligible participants included individuals aged 18 to 65 years of either gender, presenting with radiologically confirmed acute fractures of long bones, including the femur, tibia, humerus, radius, and ulna, within one week of injury. Both conservatively managed and surgically treated patients were included, provided they consented to participate and complied with follow-up visits. Patients with pathological fractures, chronic kidney or liver disease, metabolic bone disorders, parathyroid abnormalities, malignancy, or malabsorption syndromes were excluded. Additionally, patients receiving corticosteroids, anticonvulsants, or other medications affecting bone metabolism, as well as those already on vitamin D or calcium supplementation, were excluded. Cases involving severe open fractures with extensive soft tissue injury, polytrauma requiring prolonged intensive care, or patients lost to early follow-up were also excluded from the final analysis.

Following enrollment, relevant clinical and demographic data including fracture site, fracture type, mechanism of injury, gender, body mass index, comorbidities, and treatment modality were recorded using a structured proforma. Baseline biochemical evaluation was performed through venous blood sampling at admission or during the initial orthopedic assessment, prior to the initiation of any supplementation therapy. Serum 25-hydroxyvitamin D [25(OH)D] and total serum calcium levels were measured using standardized laboratory methods. Vitamin D status was categorized as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL), while serum calcium levels were classified as normal or hypocalcemic according to institutional reference ranges.

Every patient was treated with the standard orthopedic care according to the fracture's characteristics and presentation. Follow-up assessments were conducted at regular intervals, typically at 4, 8, and 12 weeks, and continued as clinically indicated. The healing of fractures was determined by clinical and radiological measures. Clinical healing was defined by reduction in pain at the fracture site, absence of abnormal mobility, and progressive restoration of limb function or weight-bearing capacity. Radiological unification was established by use of serial plain radiographs that showed bridging callus formation over the fracture site and regain of cortical continuity. The primary outcome measure was time to fracture healing, defined as the duration (in weeks) from initiation of treatment to radiographic evidence of satisfactory union. The secondary outcome was functional recovery, assessed using fracture-specific validated functional scoring systems that evaluated the patient's ability to perform daily activities and regain limb function.

Delayed fracture healing was operationally defined as prolongation of the expected healing duration based on fracture type and location, accompanied by inadequate radiological progression. Functional outcomes were categorized as satisfactory or suboptimal based on standard scoring thresholds. Serum vitamin D deficiency and

hypocalcemia was considered the primary independent variables influencing healing dynamics and functional outcomes.

Data were entered and analyzed using SPSS version 26.0. Continuous variables, including age, serum vitamin D levels, serum calcium levels, healing time, and functional scores, were expressed as mean ± standard deviation, while categorical variables, such as gender, fracture site, vitamin D status, calcium status, and healing outcomes, were presented as frequencies and percentages. Independent sample t-tests or one-way analysis of variance (ANOVA) were used for comparison of continuous variables, while the chi-square test was applied for categorical variables. Correlation analysis was performed to assess the relationship between biochemical parameters and healing outcomes. Multivariate logistic regression analysis was conducted to identify independent predictors of delayed fracture healing and poor functional recovery after adjusting for potential confounders, including age, gender, fracture site, and treatment modality. A p-value of <0.05 was considered statistically significant.

The study was conducted in accordance with established ethical standards for human subject research. Ethical approval was obtained from the Institutional Review Board/Ethical Review Committee of Nishtar Medical University, Multan, Pakistan (Ref No: 8713/NMU). prior to study initiation. Written informed consent was obtained from all participants before enrolment. Confidentiality and anonymity of patient data were strictly maintained throughout the study, and participants were informed of their right to withdraw at any stage without affecting their clinical care.

RESULTS

The study included 160 patients, mean age of the study population was 42.6 years, with the majority of participants being male (n = 98, 61.3%) compared to female (n = 62, 38.7%). Most fractures involved the lower limb bones, particularly the tibia (n = 102, 63.8%) and femur, whereas upper limb fractures accounted for 36.2% (n = 58) of cases. The most common mechanisms of injury were road traffic accidents, followed by falls and sports-related trauma. These demographic characteristics are representative of a typical orthopedic trauma patient population and are summarized in Table 1.

Biochemical analysis revealed a high prevalence of micronutrient deficiencies among the study participants. Vitamin D deficiency (<20 ng/mL) was identified in 92 patients (57.5%), while 38 patients (23.8%) had vitamin D insufficiency (20–29 ng/mL), and 30 patients (18.7%) had sufficient levels (>30 ng/mL). Similarly, hypocalcemia was observed in 56 patients (35.0%), whereas 104 patients (65.0%) had normal serum calcium levels. These findings indicate that a substantial proportion of fracture patients had suboptimal bone-related biochemical status, as presented in Table 2.

Analysis of fracture healing outcomes demonstrated a statistically significant association between serum vitamin D levels and time to union. Patients with sufficient vitamin D levels had a shorter mean healing time (9.1 ± 1.7 weeks) compared with those with insufficiency (10.4 ± 2.0 weeks) and deficiency (11.9 ± 2.5 weeks), with a highly significant difference ($p < 0.001$). A similar pattern was observed for serum calcium levels, as patients with normal calcium experienced shorter healing times (9.8 ± 1.9 weeks) compared with hypocalcemic patients (11.5 ± 2.4 weeks; $p = 0.002$). These findings emphasize the importance of optimal biochemical status in promoting timely fracture healing.

Functional recovery outcomes also varied significantly across biochemical categories. Patients with sufficient vitamin D levels achieved better functional scores (86.2 ± 6.1) compared with vitamin D–deficient patients (71.8 ± 9.2; $p < 0.001$). Likewise, normal serum calcium levels were associated with superior functional performance (82.7 ± 7.4) compared with hypocalcemia (74.1 ± 8.6; $p = 0.003$). These differences highlight the clinical importance of vitamin D and calcium in restoring functional capacity in addition to radiological recovery. These associations are summarized in Table 3.

Further statistical analysis using multivariate logistic regression demonstrated that vitamin D deficiency (Adjusted Odds Ratio [AOR] = 3.1, $p = 0.001$) and hypocalcemia (AOR = 2.6, $p = 0.004$) were independent predictors of delayed fracture healing, even after adjustment for confounding factors such as age, sex, fracture type, and treatment modality. Both deficiencies were associated with a significantly increased risk of prolonged healing time and poorer functional outcomes.

Figure 1 demonstrates that vitamin D deficiency and hypocalcemia were significant independent predictors of delayed fracture healing after adjustment for potential confounding variables. Vitamin D deficiency showed the strongest association with prolonged healing, followed by hypocalcemia.

Overall, the findings demonstrate a clear and statistically significant association between serum vitamin D and calcium levels and both fracture healing duration and functional recovery. The clinical relevance of these parameters in fracture management was evident, as patients with adequate biochemical status experienced faster union and better functional outcomes.

Table 1: Baseline Demographic and Clinical Characteristics (n = 160)

Variable	Frequency (%) / Mean ± SD
Age (years)	42.6 ± 13.1
Male	98 (61.3%)
Female	62 (38.7%)
Lower limb fractures	102 (63.8%)
Upper limb fractures	58 (36.2%)
Surgical management	96 (60.0%)
Conservative management	64 (40.0%)

Table 2: Distribution of Serum Vitamin D and Calcium Levels (n = 160)

Parameter	Frequency (%)
Vitamin D Deficient (<20 ng/mL)	92 (57.5%)
Vitamin D Insufficient (20–29 ng/mL)	38 (23.8%)
Vitamin D Sufficient (≥30 ng/mL)	30 (18.7%)
Hypocalcemia	56 (35.0%)
Normal Calcium	104 (65.0%)

Table 3: Association of Vitamin D and Calcium Levels with Healing Time and Functional Recovery

Variable	Healing Time (weeks)	Functional Score	p-value
Vitamin D Sufficient	9.1 ± 1.7	86.2 ± 6.1	<0.001
Vitamin D Insufficient	10.4 ± 2.0	78.5 ± 7.3	0.002
Vitamin D Deficient	11.9 ± 2.5	71.8 ± 9.2	<0.001
Normal Calcium	9.8 ± 1.9	82.7 ± 7.4	0.002
Hypocalcemia	11.5 ± 2.4	74.1 ± 8.6	0.003

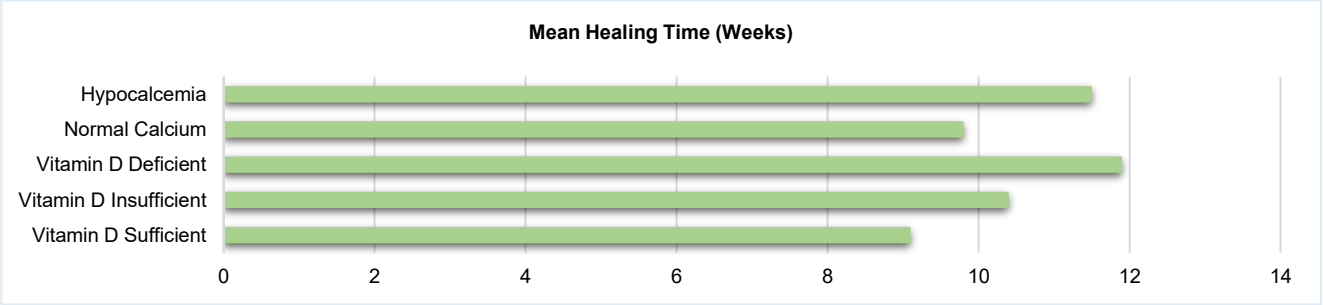

Figure 1: illustrates the multivariate regression model identifying vitamin D deficiency and hypocalcaemia as significant predictors of delayed fracture healing

DISCUSSION

The present study demonstrates a strong clinical association between serum vitamin D and calcium levels and both fracture healing duration and functional recovery in adult patients [1]. The findings showed that patients with sufficient vitamin D levels and normal serum calcium experienced faster fracture healing and better functional outcomes compared with those who had biochemical deficiencies. These results support the important role of micronutrient status in bone regeneration and fracture rehabilitation [2,3].

Fracture healing is a biologically demanding process that requires optimal mineral availability and hormonal regulation [4]. Vitamin D enhances intestinal calcium absorption and stimulates osteoblastic activity, both of which are essential for fracture callus formation and mineralization. In the present study, patients with adequate vitamin D levels had a significantly shorter healing duration than those with vitamin D deficiency. This finding is consistent with previous clinical studies reporting delayed fracture healing and increased rates of non-union among patients with hypovitaminosis D. Impaired callus mineralization in vitamin D–deficient states may explain the prolonged healing times observed in such patients [5].

Similarly, serum calcium was found to play a significant role in fracture healing. Hypocalcemic patients exhibited slower fusion and worse functional recovery [6]. Calcium is a key structural component of hydroxyapatite crystals, which provide mechanical strength to newly formed bone. The metabolic demand for calcium increases substantially during fracture repair, and inadequate calcium availability may impair callus maturation. These findings are consistent with previous studies showing that calcium deficiency adversely affects bone remodeling and structural integrity during healing [7].

It is also important to highlight the inclusion of functional recovery as an additional outcome measure in this study, beyond radiological healing alone [8]. Higher serum levels of both vitamin D and calcium were associated with better functional outcomes and a faster return to normal daily activities. These findings emphasize the importance of patient-centered outcomes and further support the need for orthopedic studies that incorporate functional recovery as a key endpoint [9].

It is also noteworthy that a high prevalence of vitamin D deficiency and hypocalcemia was observed among the study participants (57.5% and 35.0%, respectively) [10]. These findings are consistent with regional data from South Asian populations, where micronutrient deficiencies and low vitamin D levels are highly prevalent due to a combination of nutritional, environmental, and lifestyle-related factors. Such deficiencies may partly explain the variability in fracture healing outcomes observed in routine clinical practice [11].

The multivariate analysis performed in the present study further demonstrated that vitamin D deficiency and hypocalcemia were independent predictors of delayed fracture healing, even after adjustment for potential confounding variables. These findings indicate a clear association between the evaluated biochemical parameters and fracture healing outcomes [13,14]. Nevertheless, fracture healing is a multifactorial process, and several additional factors including age, vascularity, fracture type, and mechanical stability may also influence healing outcomes [15].

Despite the encouraging findings, several limitations of the study should be acknowledged [16]. First, the study was conducted at a single center, which may limit the generalizability of the results. Second, although the sample size was adequate to support the main findings, smaller effects may not have been fully detected. In addition, the study did not evaluate the effect of vitamin D or calcium supplementation on healing outcomes, which could provide important therapeutic insight.

Future research should focus on multicenter randomized controlled trials to determine whether correction of vitamin D and calcium deficiencies can accelerate fracture healing and improve functional recovery. These biochemical parameters may provide a useful foundation for the incorporation of targeted nutritional optimization into fracture management protocols, offering a potentially cost-effective and clinically valuable strategy [17,18].

CONCLUSION

Serum vitamin D and calcium levels have a significant influence on fracture healing and functional recovery in adult patients. Deficiency of these micronutrients is associated with delayed fracture healing and poorer functional outcomes. Careful assessment and timely correction of vitamin D and calcium deficiencies may be beneficial in enhancing healing rates and improving overall clinical recovery in patients with fractures.

Conflict of Interest: The authors declare no conflicts of interest.

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Authors' Contributions: M.H.K. contributed to conceptualization, study design, and manuscript drafting. M.A.K. was responsible for data collection, patient follow-up, and data acquisition. M.A. performed data analysis, interpretation of results, and manuscript editing. M.H.K. contributed to supervision, critical revision, and final approval of the manuscript. All authors approved the final version of the manuscript.

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Data Availability: The datasets generated and analyzed during this study are available from the corresponding author upon reasonable request.

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