



Original Research

High Rates of Vitamin D Deficiency in Acute Rehabilitation Patients



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KEYWORDS

Rehabilitation;
Vitamin D;
Vitamin D deficiency;
Inpatients;
Hospitalization

Abstract Objective: To determine the prevalence of low vitamin D (<30 ng/mL), including vitamin D insufficiency (20-29.9 ng/mL) and deficiency (<20 ng/mL), in an acute rehabilitation setting.

Design: Cross-sectional, retrospective cohort study.

Setting: University-affiliated inpatient rehabilitation facility (IRF) at a metropolitan county hospital.

Participants: Patients (N=100; 64 men/36 women), aged 19-92 years (mean, 62±18.9y), who were admitted to and discharged from an IRF over a 6-month study period. The most frequent admitting diagnoses included stroke (n=11), brain injury (n=36), spinal cord injury (n=14), and polytrauma (n=10).

Interventions: Not applicable.

Main Outcome Measures: Serum vitamin-25 (OH)D level at admission to the IRF.

Results: Of 100 patients, 76% had low vitamin D (<30 ng/mL), with 29% demonstrating vitamin D insufficiency (20-29.9 ng/mL) and 47% demonstrating vitamin D deficiency (<20 ng/mL). Younger patients demonstrated higher rates of vitamin D deficiency compared with older patients ($P<.0001$).

Conclusions: Low vitamin D is common in patients admitted to the IRF, with rates more than double those reported in the general population among individuals younger than 45 years. The current results suggest that the IRF setting may be a favorable checkpoint to screen for and initiate treatment of low vitamin D and optimize rehabilitation outcomes.

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List of abbreviations: BMI, body mass index; IRF, inpatient rehabilitation facility.

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Vitamin D is an essential mediator of calcium metabolism throughout the body. Although the association between vitamin D, bone health, and fracture risk is well known, vitamin D status also has implications in wide-ranging systems beyond the skeletal system.¹ Low vitamin D (<30 ng/mL) has been associated with increased risk of cardiovascular disease,² malignancy,³ depression,⁴ and autoimmune diseases.^{5,6} In addition to fracture risk, low vitamin D is associated with increased risk of progression in musculoskeletal pain^{7,8} and decreased muscle strength.⁹

Recent studies report the reemergence of vitamin D deficiency as a global health concern.¹⁰ Among the general population, global rates of vitamin D deficiency in healthy adults range from 1%-80%.¹¹ In the United States, a large scale study of community-dwelling adults reported rates of vitamin D deficiency as high as 41%, with the highest rates noted in African American individuals; Hispanic individuals; individuals without college education; and those who are obese, have hypertension, have low high-density lipoprotein levels, and are in poor health.¹²

The inpatient rehabilitation patient has multiple risk factors for low vitamin D, including cardiovascular disease, hypertension, diabetes, and malignancy. Compared with patients discharged directly to home, inpatient rehabilitation patients are older, have more medical comorbidities, and have more functional deficits, including decreased mobility.¹³ Given a previous study suggesting that vitamin D supplementation reduced the risk of falls in institutionalized individuals,¹⁴ the inpatient rehabilitation setting is potentially a prime juncture to recognize and treat functionally relevant low vitamin D.

Previous studies evaluating the rates of low vitamin D in the acute rehabilitation setting are limited. The current study examined rates of low vitamin D (<30 ng/mL), including vitamin D insufficiency (20-29.9 ng/mL) and deficiency (<20 ng/mL) in an acute rehabilitation setting at a metropolitan academic medical center. Secondary analyses evaluated associations between low vitamin D and demographic as well as other clinical factors.

Methods

Study design

A cross-sectional, retrospective study to evaluate rates of low vitamin D (<30 ng/mL), including both vitamin D insufficiency (20-29.9 ng/mL) and deficiency (<20 ng/mL), in patients admitted to an inpatient rehabilitation facility (IRF). Patients were excluded from the study if they were aged <18 years, pregnant, or taking vitamin D supplementation prior to IRF admission. The study protocols were approved by the university institutional review board. Consent for chart review was waived. The STROBE cross-sectional checklist was used to write the current report.¹⁵

Study protocol

Vitamin D status was assessed at admission for patients admitted to and discharged from the university-affiliated IRF from March 2019 to September 2019. Subsequent

encounters in patients readmitted during the study period of interest were excluded from study. The primary outcome measure was vitamin D status, testing the hypothesis that patients admitted to IRF would demonstrate higher rates of low vitamin D (<30 ng/mL) compared with rates reported in healthy, community-dwelling adults. Secondary analyses evaluated associations between vitamin D status, demographic variables (age, sex, ethnicity), and clinical variables (body mass index [BMI], admitting diagnosis, pre-IRF length of acute hospitalization, presence of fractures, treatment with antiepileptics, treatment with systemic steroids).

In line with clinical practice guidelines published by the Endocrine Society in 2011,¹⁶ patients who were vitamin D deficient (<20 ng/mL) were treated with 50,000 IU of vitamin D2 once a week for 8 weeks, with instructions to follow up with a primary care provider after discharge. During the study period, oral vitamin D supplementation was well tolerated, and no adverse effects were identified or reported.

Measurements

Vitamin D status was determined from blood serum levels of total serum 25(OH)D using an immunoassay.^{17,a} The lower limit of the immunoassay for serum vitamin D was 7. For patients in whom vitamin D levels were undetectable, a value of 7 was assigned for statistical calculations. Calcium, phosphorus, and magnesium levels were also determined from blood serum samples. Reference ranges are provided in [table 1](#).

Data analysis

Bivariate analyses between vitamin D level and continuous variables (age, BMI, pre-IRF length of acute hospitalization) were performed using 2-tailed linear regression models. Analyses between vitamin D level and categorical variables (sex, ethnicity, admitting diagnosis, presence of fractures, treatment with antiepileptics, treatment with systemic steroids) were performed using 1-way analysis of variance. Analyses between vitamin D level and categorical variables were performed using the chi-square test. Parametric statistical methods were used because all measures were normally distributed or could be transformed to a normal distribution. Statistical significance was set at $P < .05$, with Bonferroni correction for multiple comparisons. Statistical tests were performed using R,¹⁸ version 3.6.1.^b

Table 1 Reference ranges for serum 25(OH)D, calcium, phosphorus, and magnesium

| Serum Measurement | Lower Limit | Upper Limit |
|------------------------|-------------|-------------|
| 25-OH vitamin D, ng/mL | | |
| Sufficient | 30.0 | 100.0 |
| Insufficient | 20.0 | 29.9 |
| Deficient | | 19.9 |
| Calcium, mg/dL | 8.6 | 10.3 |
| Magnesium, mg/dL | 1.9 | 2.7 |
| Phosphorus, mg/dL | 2.5 | 5.0 |

Results

Study cohort

A total of 115 unique patients were admitted to IRF during the study period. Nine patients did not have vitamin D levels as part of admission labs owing to insufficient specimen or systematic errors in admission orders. Of the remaining 106 patients, 6 were already receiving vitamin D supplementation either as part of home medications or as part of treatment initiated during the acute hospitalization. Excluding patients who did not have admission vitamin D level ($n=9$) and those already receiving vitamin D supplementation prior to IRF admission ($n=6$), the subsequent study sample included 100 patients (from 115 contiguous and unique patients admitted and with 15 excluded from study). The study cohort was aged 19-92 years with a mean age of 62.0 ± 18.9 years; 36% were women. Demographic and clinical characteristics of the study sample are provided in [table 2](#).

Vitamin D status

The study sample had a mean vitamin D level of 24.6 ± 13.8 ng/mL. In total, 76 individuals demonstrated low vitamin D levels (<30 ng/mL), with 47 in the deficient (<20 ng/mL) range and 29 in the insufficient (20-29.9 ng/mL) range. Three individuals had undetectable levels of serum 25(OH)D (<7 ng/mL).

Age was associated with vitamin D status

There was a statistically significant association between age and low vitamin D (<30 ng/mL; $t=5.46$; $P<.0001$). There was also a statistically significant association between younger age and higher rates of vitamin D deficiency (<20 ng/mL; $t=4.12$; $P<.0001$). When the study sample was subdivided into 5 contiguous age subgroups, vitamin D deficiency was proportionally higher in younger subgroups compared with older subgroups ([fig 1](#)).

Table 2 Characteristics of study sample

| Characteristic | 25 (OH)D <30 ng/mL | 25 (OH)D ≥ 30 ng/mL | P Value |
|--|----------------------|--------------------------|----------|
| Age, mean \pm SD | 58.0 ± 19.2 | 74.8 ± 10.6 | $<.0001$ |
| <31 y, n (%) | 10 (100) | 0 | |
| 31-45 y, n (%) | 12 (100) | 0 | |
| 46-60 y, n (%) | 11 (79) | 3 (21) | |
| 61-75 y, n (%) | 25 (76) | 8 (24) | |
| >75 y, n (%) | 18 (58) | 13 (42) | |
| Sex, n (%) | | | .25 |
| Female | 25 (69) | 11 (31) | |
| Male | 51 (80) | 13 (20) | |
| Ethnicity, n (%) | | | .73 |
| Non-Hispanic | 56 (76) | 18 (24) | |
| Hispanic | 19 (79) | 5 (21) | |
| BMI, mean \pm SD | 26.0 ± 6.0 | 26.5 ± 6.9 | .73 |
| Admitting diagnosis, n (%) | | | .67 |
| Stroke | 11 (85) | 2 (15) | |
| TBI | 6 (67) | 3 (33) | |
| Nontraumatic brain injury | 15 (83) | 3 (17) | |
| Traumatic SCI | 2 (100) | 0 | |
| Nontraumatic SCI | 12 (67) | 6 (33) | |
| Other neurologic conditions* | 7 (70) | 3 (30) | |
| Other orthopedic conditions† | 3 (75) | 1 (25) | |
| Polytrauma with and without TBI | 10 (83) | 2 (17) | |
| Burn | 0 | 1 (100) | |
| Miscellaneous‡ | 10 (77) | 3 (23) | |
| Pre-IRF length of acute hospitalization, mean \pm SD | 9.33 ± 9.11 | 6.46 ± 5.90 | .08 |
| Presence of acute fractures, n (%) | | | .08 |
| Yes | 19 (90) | 2 (10) | |
| No | 57 (72) | 22 (28) | |
| Treatment with antiepileptics, n (%) | | | .79 |
| Yes | 17 (74) | 6 (26) | |
| No | 59 (77) | 18 (23) | |
| Treatment with systemic steroids, n (%) | | | .18 |
| Yes | 11 (92) | 1 (8) | |
| No | 65 (74) | 23 (26) | |

Abbreviations: SCI, spinal cord injury; TBI, traumatic brain injury.

* Other neurologic conditions included multiple sclerosis ($n=1$), Parkinsonism ($n=2$), and neuromuscular disorders ($n=1$).

† Other orthopedic conditions included unilateral hip fracture ($n=2$).

‡ Miscellaneous conditions included cardiac disorders ($n=4$), debility ($n=2$), surgical complications ($n=1$), neoplasm ($n=5$), and infection ($n=1$).

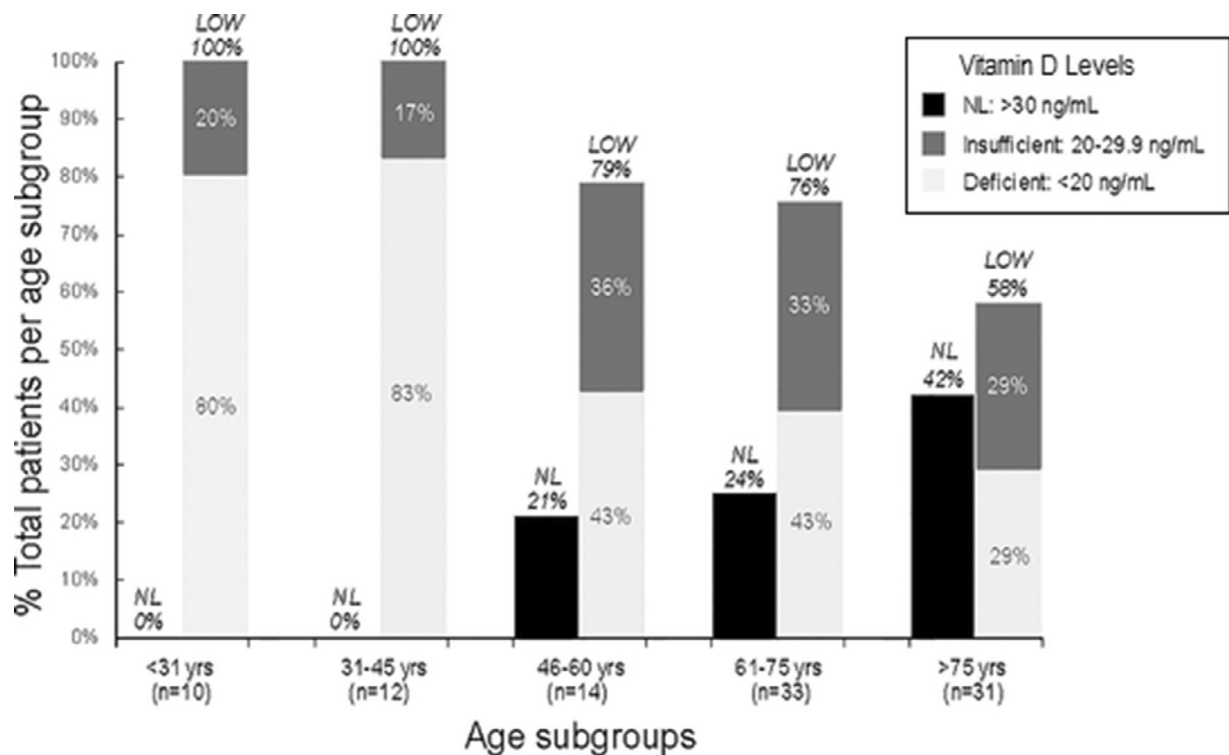


Fig 1 Percentage of patients with sufficient (NL, >30 ng/mL, black bar) and low (<30 ng/mL, second bar) vitamin D level in 15-year contiguous age subgroups at IRF admission. Proportions of patients with low vitamin D level were further subdivided into vitamin D level insufficient (20-29.9 ng/mL, dark gray) and deficient (<20 ng/mL, light gray) subgroups. Number of patients per subgroup are detailed in the horizontal axis. NL, normal level.

Sex, ethnicity, BMI, admitting diagnosis, pre-IRF length of acute hospitalization, presence of acute fractures, treatment with antiepileptic medications (including levetiracetam, lamotrigine, and carbamazepine), and treatment with systemic steroids (including dexamethasone and prednisone) did not demonstrate statistically significant associations with vitamin D status ($P>.05$) (see [table 2](#)). Concurrent hypocalcemia, hypophosphatemia, hypomagnesemia, and hypermagnesemia were also not associated with low vitamin D (<30 ng/mL; $P>.05$). There was a statistical association between low vitamin D and hyperphosphatemia ($\chi^2=6.30$; $P=.012$), which did not survive Bonferroni correction.

Multivitamin cotreatment

Of the 100 patients included in the study sample, 19 individuals either reported taking multivitamins before acute hospital admission or were started on multivitamin treatment during the acute hospitalization prior to IRF admission. Compared with those not taking a multivitamin before IRF admission, there was not a statistically significant difference between groups with respect to rates of low (<30 ng/mL), insufficient (20-29.9 ng/mL), or deficient (<20 ng/mL) vitamin D. Furthermore, the groups did not differ with respect to pre-IRF length of acute hospitalization, age, sex, BMI, presence of fractures, treatment with antiepileptic medications, or treatment with systemic steroids. There was a statistical difference between groups with respect to ethnicity ($\chi^2=3.96$; $P<.05$), which did not survive Bonferroni correction.

Discussion

The current study evaluated the rates of low vitamin D in patients admitted to IRF. Overall, 76% of patients had low vitamin D (<30 ng/mL), with 47% in the deficient range (<20 ng/mL) and 29% in the insufficient range (20-29.9 ng/mL). Individuals who were younger were more likely to be vitamin D deficient, but other demographic and clinical covariates, including sex, BMI, hypocalcemia, hypophosphatemia, hypomagnesemia, presence of fractures, and treatment with systemic steroids were not significantly associated with low vitamin D.

There are limited previous studies evaluating rates of low vitamin D in an IRF setting. As per Kiebzak et al,¹⁹ 11% of patients with stroke, acute fracture, and hip or knee replacement admitted to an inpatient rehabilitation unit were vitamin D deficient. Conversely, a group of patients admitted to a subacute rehabilitation facility were 49.1% vitamin D deficient,²⁰ a rate similar to that described in the current report. Differences in reported rates of vitamin D deficiency likely reflect the changes in inpatient rehabilitation patient cohorts in response to federal regulatory changes affecting IRF reimbursement systems.²¹ As a result, the current acute rehabilitation patient is significantly less likely to be admitted after lower-limb joint replacement, as seen by Kiebzak et al (38 of 77 patients).¹⁹ In contrast, the current study describes a group with primarily neurologic disorders (including stroke, brain injury, and spinal cord injury) who required longer acute hospitalizations, suggesting that the current group represents a sicker and more functionally-debilitated inpatient rehabilitation cohort compared with that previously reported.

The current study is presented on the backdrop of recently updated recommendations on vitamin D deficiency screening in adults by the US Preventive Services Task Force.²² Although the Task Force currently recommends against population-based vitamin D deficiency screening in community-dwelling, nonpregnant adults, the recommendation statement also specifies that this recommendation excludes individuals who are hospitalized. The recommendation also excludes those with signs or symptoms of vitamin D deficiency, including muscle weakness, such as functionally impaired patients admitted to IRF. The supposition that vitamin D deficiency is related to degree of functional impairment is supported by previous studies demonstrating vitamin D levels to be correlated with IRF length of stay.¹⁹ Consequently, the current study reinforces findings from a previous report by Sari et al¹⁴ demonstrating particularly high rates of low vitamin D in IRF patients admitted with neurologic diagnoses.

The functional implications of low vitamin D levels are underpinned by its association with overall musculoskeletal physiology. Low vitamin D (<30 ng/mL) has been shown to cause reversible proximal myopathy through type II fiber atrophy and decreased protein synthesis.²³ Functionally, patients with low vitamin D demonstrate reduced grip strength, decreased lower extremity function, sarcopenia, and increased body sway.²⁴ Together, impairments relating to low vitamin D result in increased risk of falls and decreased functional capacity. Indeed, in a US study of 4100 ambulatory older adults (age >60y), low vitamin D was shown to increase time to completion on the 8-foot walk test and the sit-to-stand test.²⁵ Fortunately, the deleterious effects of low vitamin D on the musculoskeletal system are potentially reversible. In the osteoporotic and osteopenic patient population, calcium and vitamin D supplementation reduces fracture risk,²⁶⁻²⁸ whereas vitamin D supplementation in patients with hemiplegia poststroke was shown to accelerate balance recovery and improve overall functional capacity.¹⁴ Finally, a meta-analysis of individuals with a mean age >65 years receiving supplemental vitamin D found that both supplemental and active forms of vitamin D reduced fall risk by up to 26%.²⁹

The current study found that age was inversely associated with low vitamin D status, such that rates of vitamin D <30 ng/mL were 100% among those who were aged <45 years on IRF admission. Given that the half-life of vitamin D is approximately 2-3 weeks¹⁶ and that the average pre-IRF length of stay in the currently reported group was 9.33 days, low vitamin D in younger patients admitted to IRF after acute hospitalization is likely a premorbid condition. This finding is consistent with recent reports demonstrating surprisingly high rates of vitamin D deficiency among young adults, particularly those with central obesity.^{30,31} Furthermore, as demonstrated in the current group in which younger individuals were more likely to be admitted to IRF owing to polytrauma resulting in multiple acute fractures, these findings provide support for routine screening of vitamin D deficiency in younger individuals admitted to IRF for polytrauma.

Secondary measures, including ethnicity and BMI, did not correlate with vitamin D status. Prior reports have shown a higher incidence of low vitamin D (<30 ng/mL) in ethnic minorities compared with their White counterparts.^{32,33} In the current study, there was a trend demonstrating that

Hispanic patients had a higher prevalence of low vitamin D compared with non-Hispanic patients. However, the association was not statistically significant and may reflect an oversimplification of the ethnicity classifications in the current study design. Although previous studies report associations between low vitamin D, adiposity, and obesity-related chronic diseases,^{33,34} the cohort demonstrating low vitamin D in the current study had an average BMI that did not fall within the obese range.

There were no observed differences in the prevalence of low vitamin D in patients receiving antiepileptic or steroid therapy. Long-term treatment with antiepileptics has been found to have negative effects on bone health including decreasing bone density, altering bone metabolism biochemically, modifying bone turnover markers, and increasing fracture risk,³⁵ resulting in osteomalacia, hypocalcemia, hypophosphatemia, and decreased levels of vitamin D metabolites. In the current study, antiepileptic therapy was primarily administered for seizure prophylaxis in the setting of acute injury. As a result, the short duration of antiepileptic treatment combined with a relatively small patient cohort of patients receiving antiepileptic or steroid medication likely resulted in an underpowered analysis of the relationship between antiepileptic or steroid therapy and vitamin D status.

Study limitations

The current study design and results have multiple limitations. As a cross-sectional and retrospective study, the findings reported represent associations and not causal relationships. Future studies that include comparative analyses examining differences in vitamin D status between IRF patients and a matched cohort of healthy, community dwelling individuals are needed to determine rates of low vitamin D accounting for regional covariates, including latitude, ethnic diversity, and dietary supplementation. In addition, longitudinal studies are needed to determine the effect of vitamin D supplementation on risk of falls, fractures, and functional outcomes after IRF discharge; patient compliance with prescribed supplementation and follow-up care; as well as long-term side effects or adverse events associated with supplementation.

Conclusions

In a cohort of 100 patients admitted to an acute rehabilitation unit after acute care, the rate of low vitamin D (<30 ng/mL) was 76%, with 47% of patients demonstrating vitamin D deficiency (<20 ng/mL).²² The present report demonstrates high rates of vitamin D deficiency in the IRF setting and lends support toward classifying the inpatient rehabilitation patient as an at-risk population for vitamin D deficiency. As such, the IRF setting may be a prime junction for identifying and initiating treatment for functionally relevant vitamin D deficiency.

Suppliers

- Immunoassay; Beckman Coulter.
- R, version 3.6.1; R Foundation for Statistical Computing.

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