

Vitamin D Deficiency and Hip Fractures: 2020-2022

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Abstract

Introduction: Hip fractures remain highly prevalent oftentimes life-threatening events among older populations, despite years of multiple related preventive endeavors.

Objectives: This mini-review strove to examine whether: 1) A vitamin D deficiency is an important hip fracture determinant in the older adult population, and 2) whether more consideration of this vitamin is warranted clinically.

Methods: Relevant current data concerning this topic were sought from three well-established preselected electronic data bases housing current English language research or analytic reports pertaining to the examination of the possible association of the presence of a vitamin D deficiency among older hip fracture surgical patients and its probable clinical implications. Reviewed specifically were representative recent studies and reviews published between January 1, 2020 - February 28, 2022 (post COVID-19 period), including their findings and key conclusions.

Results: Most current articles tend to support an association between low vitamin D levels and the presence of an injury induced hip fracture in a high percentage of older affected adults. As well, those who perform more poorly post-hip fracture surgery appear to often suffer from a lower than desirable vitamin D serum level. Having a COVID-19 diagnosis, an independent hip fracture correlate, may implicate a vitamin D deficiency.

Conclusion: More intense and thoughtfully designed research that evolves from the onset of the COVID-19 pandemic and post-pandemic periods may reveal the multiple ways vitamin D can mediate hip fracture occurrences and recovery, while helping to advance more successful much needed evidence based preventive practices to offset the persistent and forthcoming predicted global age-associated hip fracture burden and its immense projected associated human and social costs.

Keywords: Bone; Fractures; Hip Fractures; Intervention; Prevention, Supplementation, Vitamin D Deficiency

Introduction

According to Emmerson., *et al.* [1] fractures of the hip, common among the elderly, a population that is growing rapidly, alongside growing hip fracture numbers [2], are both painful as well as costly due to their multiple disabling, impacts and outcomes, as well as being associated with high rates of premature mortality [3], independence losses, possible long-term nursing home requirements

and secondary fractures [4,5]. However, although commonly attributable to falls related injuries that are most severely impactful in the case of any underlying bone fragility, to date, hip fracture preventive programs that mostly focus on falls prevention, including balance and strength training, plus drug assessments and various pharmacologic, dietary and environmental management strategies remain less than optimally effective as a whole. Additionally, it is highly possible that since the onset of the corona virus 19 (COVID-19) pandemic in December 2019, more older adults will have sustained hip fracture injuries in the home due to isolation effects, movement or mobility, restrictions, service closures, and limited availability of foods/sunlight exposure [6] or vitamin D [7] than anticipated. In this respect some evidence points to consistently high hip fracture admission rates emanating from falls injuries occurring in the home, even though other fractures have abated, and those hip fracture cases who sustain COVID-19 infections are not only highly prone to premature mortality independent of any other factor, but are often those with low vitamin D serum levels [7]. At the same time even though prior data show vitamin D deficits are highly prevalent among high risk populations [8], much controversy has surrounded whether this is a hip fracture correlate, and even more contentious is a possible preventive or moderating role for vitamin D supplementation in select cases. But is there current supportive evidence of a possible favorable impact of vitamin D, or its variants on mitigating hip fracture injuries, and on fostering functional recovery and survival post hip fracture especially among older adults with a history of osteoporosis [9]? Moreover, if as Neale, *et al.* [10] argue that a vitamin D deficiency is associated with an increased risk of falls and fractures, is this association potentially causal?

Aims of Review

Since bone fractures, such as those that occur readily at the hip joint in older populations may be affected to a considerable degree in the face of deficient vitamin D, this current mini review aimed to examine the most recent data on this issue since the COVID-19 pandemic may have altered the nature of the degree to which prior findings may be currently relevant. It also aimed thereby to establish whether a need exists for more continuous targeted research in this realm, and if so in what regard.

Methods

To obtain the desired data to fulfill the study aims, an extensive scan of available documents housed in the PUBMED, Scopus, and WEB OF SCIENCE CONSOLIDATED, including most full length articles published in English and derived from research conducted as of January 1 2020 up until March 1 2022 using the key terms Vitamin D Deficiency and Hip Fractures was sought.

After scanning the available article listings found on these websites for potential inclusion in this current mini-review, those that addressed some aspect of the current topic of interest and were less than 2 years old, were specifically selected, downloaded and scrutinized in more depth by the author without regard to research design. After reviewing the available data, it was clear that no systematic overview of such a limited diverse data base was possible and would not be of sufficient value for definitively advancing current practice or research. Hence, while it is acknowledged that the present body of data may not be exhaustive-and that others have attempted meta-analyses or aggregate reviews on a similar theme, it was felt a more qualitative descriptive approach was the only approach that could possibly help to highlight any trends and tentative conclusions regarding this relatively uncharted topic. To this end, a narrative description of the material deemed to meet the basic review aims is presented, rather than any aggregated approach. Excluded were articles on hip fractures in particular health conditions, those that did not discuss hip fractures in the older adult, and non English articles. The term vitamin D was applied to represent all data pertaining to vitamin D but where different formulae may have been applied.

Results and their Analysis

General observations

As of January 1 2020, the data examined and covering all years with no restrictions revealed 144 possible related postings directly related to the current topic as of February 28, 2022 (See table 1).

Key Words	Data Base		
	PUBMED	SCOPUS	Web of Science
Hip Fractures	6393	8523	8004
Vitamin D	11451	19019	17204
Hip Fracture Prevention Strategies	136	99	146
Vitamin D + Osteoporosis	923	998	1366
Vitamin D + Hip Fractures	180	532	435
Vitamin D + Falls	186	314	375
Vitamin D Deficiency + Hip Fractures	63	144	129
Vitamin D Supplementation + Hip Fractures	45	147	116

Table 1: Summary of numbers of articles posted at key data bases as reported between January 1, 2020-March 2022 showing variations across and within databases as regards current topic and related themes, with very few focused on either prevention or vitamin D deficiency and hip fractures.

A further examination of the available studies revealed that regardless of data base, the relevant clinical studies on the current topic appeared to mostly be housed in PUBMED with few exceptions and that these show low vitamin D levels are commonly observed in admitted elderly hip fracture cases. Moreover, among the available clinical studies, it appears the presence of low vitamin D impacts the recovery processes post surgery, regardless of study approach and sample. As well, many advocate screening for vitamin D to verify the presence of any need to intake dietary sources or vitamin D supplements.

Research observations

Based on studies showing vitamin D may play a critical role in the proliferation and differentiation of skeletal muscle and bone metabolism [11], a role for vitamin D in influencing hip fracture risk, as well surgical outcomes was posited. In this regard, Kim., *et al.* [11] who examined the prevalence of vitamin D deficiency in 70 elderly patients undergoing hip fracture surgery alongside with 100 cases undergoing elective primary total hip arthroplasty surgery found serum vitamin D levels were lower, and the percentages of patients with vitamin D insufficiency and deficiency were higher in the hip fracture group. A vitamin D deficiency was also more prevalent in those who were sarcopenic when compared to those who were not, thus implying some association between muscle and bone mass decrements in a sub group of hip fracture cases that may be linked to low vitamin D levels. However, as outlined by Moo., *et al.* [12] their findings showing 91.7% of 796 hospitalized elderly patients with hip fracture had inadequate vitamin D level, also showed this finding was not related to other factors such as numbers of comorbid illnesses, age, gender, fracture type, and smoking history, implying vitamin D deficits may be independently associated with hip fractures among certain older populations.

Given that low concentrations of vitamin D are considered one of the risk factors for hip fracture and can be demonstrated to be lower than desired when assessed prior to hip fracture surgery and for some time after [13], as well as being associated with less desirable outcomes, Lim., *et al.* [14] sought to compare a vitamin D deficient group and vitamin D sufficient group and assess the extent of any possible clinically significant association between the presence of a preoperative vitamin D deficiency and the postoperative walking ability of selected cases post hip fracture surgery. In this study conducted between January 2014 and January 2020, 1,029 elderly patients with hip fracture (243 in men and 785 in women) had their preoperative serum 25-hydroxy-vitamin D3 levels measured using well accepted strategies. These emergent data showed that among the 1,029 elderly patients, 702 could be classified as representing a vitamin D de-

ficient group (< 20 ng/mL). It was also observed that the mean length of the hospital stay by those in the vitamin D deficient group was significantly longer than that recorded for the vitamin D sufficient group (27.7 ± 17.8 vs. 2.9 ± 11.8 days). As well, the mean postoperative ambulatory disability score in the deficient group was significantly higher than in the sufficient group (4.0 ± 2.1 vs. 3.1 ± 1.9 days). Vitamin D deficiency was significantly associated with a higher risk of delirium and pneumonia. In sum, the presence of a preoperative vitamin D deficiency in elderly hip fracture patients tended to prolong the duration of their hospital stay, while decreasing their postoperative ambulatory status, and possibly raising the risk of delirium and pneumonia. Accordingly, vitamin D deficiencies, which also appear to specifically increase the severity of intertrochanteric hip fracture [15], need to be sought, and if identified intervened upon in the geriatric patient with a high fracture risk profile [14].

Work by Jamal, *et al.* [16] that commenced in 2019 further showed that for cases 65 years and older 67% of their study population was suffering from some degree of vitamin D deficiency. Results further showed a significant association of vitamin D deficiency and the severity of the observed intertrochanteric fractures (p < 0.05). Moreover, a study by Ingstad, *et al.* [17] of hip fracture cases showed 872 (47%) patients had serum calcidiol levels less than 50 nmol/L, and that those patients with low vitamin D had more delirium, more new hip fractures, and more medical readmissions, but not more orthopedic complications after 1 year. According to other data, low vitamin D serum levels, common in patients with osteoporotic or brittle hip fractures [18,19], may readily produce a minimal impact hip fracture [18], as well as a high risk of falling due its negative impact on physical function [20]. Since vitamin D is an important element that helps to maintain a healthy musculoskeletal system, its deficiency may yet account for a considerable proportion of those osteoporotic fractures that occur readily in many elderly adults [20], even though information on this aspect is relatively limited and not supported by all. However, keeping an open door in this respect, along with further study is likely to prove of high relevance given that vitamin D deficiency remains widespread in the geriatric population, wherein those with hip fracture are found especially vulnerable compared to healthy cases [6] when compared to cases undergoing total hip joint replacement surgery for arthritic disability [13] and as outlined in current publications listed in table 2.

Researchers	Key findings
Arshad, <i>et al.</i> [18]	Of those cases with primary or second osteoporotic hip fractures who were screened before surgery, all were declared vitamin D deficient. All were discharged with recommendations to adhere to vitamin D supplementation.
Awal, <i>et al.</i> [21]	Routine vitamin D supplementation may be indicated in ageing patients although this may not always protect against low-energy fractures
Bischoff-Ferrari [6]	Several randomized intervention trials, comparing 800-1000 IU vitamin D/day versus placebo or calcium, showed a significant reduction in falls and hip fractures in adults ≥65 years of age who had an increased risk of vitamin D deficiency and of falls or fractures
Chiang, <i>et al.</i> [2]	Among 310 older adults with hip fracture, mean age 80 ± 10 years, vitamin D levels pre surgery categorized as deficient, insufficient, and sufficient yielded 180, 84, and 46 patients (or 58.1%, 27.1%, and 14.8% cases), respectively. Malnutrition was the only significant factor explaining this finding of suboptimal vitamin D serum levels.
Chevalley, <i>et al.</i> [22]	Vitamin D plays a significant role in the pathophysiology and healing of fragility fractures and post fracture rehabilitation. Correction of vitamin D deficiency should be one of the main outcomes of fracture liaison services.
Han, <i>et al.</i> [23]	Among 732 patients, vitamin D deficiency and inadequacy were high in patients with low-energy hip fractures, where only 4.9% of patients had normal vitamin D levels. These findings suggest that efforts should be made to maintain proper vitamin D concentration
Hao, <i>et al.</i> [3]	Vitamin D deficiency (<12 ng/mL) is associated with reduced ambulation after hip fracture surgery.

Hershkowitz, <i>et al.</i> [24]	Vitamin D levels were found to be significantly associated with the discharge functional independence measure score.
Ingstad, <i>et al.</i> [17]	Low vitamin D at admission for hip fracture increased the risk of delirium, a new hip fracture, and medical readmissions, but not orthopedic complications.
Jamal, <i>et al.</i> [16]	There is a strong association between degree of vitamin D deficiency and type of intertrochanteric fractures.
Kim, <i>et al.</i> [11]	Vitamin D deficiency was more prevalent in patients undergoing hip fracture surgery than in patients undergoing elective total hip arthroplasty surgery.
Lim, <i>et al.</i> [14]	Vitamin D deficiency in hip fractures patients was associated with prolonged duration of hospital stay and decrease of postoperative ambulatory status and may increase the risk of delirium and pneumonia.
Neale, <i>et al.</i> [10]	Even in sunny Australia, vitamin D deficiency contributes to a considerable number of hospitalizations as a consequence of falls and for treatment of hip fracture. In older Australians, and in countries where the prevalence of vitamin D deficiency is higher, the impact will be even greater.
Ormeño and Langenegger [25]	Lower solar radiation was associated with higher hip fracture admission rates in men from Chile. This was taken to support the idea that solar radiation, a surrogate of vitamin D, may be involved in the development of fractures in older population.
Sim, <i>et al.</i> [26]	Out of 664 hip fracture surgery patients, 9% had severe vitamin D deficiency and 39% mild deficiency at baseline before surgery. Those patients with severe vitamin D deficiency had significantly poorer baseline and 6-month mobility and physical functioning scores.
Skuladottir, <i>et al.</i> [20]	In a prospective study of 4309 subjects, serum vitamin D concentrations were positively associated with bone mineral density and femoral neck bone content, physical function, leg strength and balance indicators. Those with deficient compared to sufficient status at baseline had a higher age-adjusted risk of incurring a hip fracture.
Wang, <i>et al.</i> [2]	There is a high prevalence of vitamin D insufficiency in elderly patients with hip fractures in China. The data imply that vitamin D plays an important role in the occurrence of hip fractures in elderly patients, and especially where patients also suffer from osteoporosis.
Wong, <i>et al.</i> [9]	Compared to low serum vitamin D levels, high levels reduce the risk of hip fractures in the patients aged 60 years or older.

Table 2: Table showing possible benefits of ensuring/attaining optimal serum vitamin D levels in efforts to ameliorate hip fracture correlates.

Discussion

Hip fractures, an ongoing major health concern among aging populations may not only severely restrict mobility and independence, but may increase the risk of premature mortality. Often associated with an elevated risk of multimorbidity, possible osteoarthritic joint changes, pain, enormous medical and social costs, and slow recovery rates in survivors, it is possible associated nutritional/sunlight exposure factors such as vitamin D play a causative and/or mediating role in this negative cycle of health events as outlined by Neale, *et al.* [10] and others [3]. This is especially evident in the current literature and in spite of available pharmacologic therapies, as well as falls

prevention programs, and may be exacerbated by the impact of COVID-19 pandemic movement and access as well as isolation restrictions, although this has not been studied to any degree.

Moreover, despite a call in 2013 by Maier, *et al.* [28] to consider harnessing interdisciplinary efforts to improve vitamin D supplementation in seniors both before a hip fracture occurs and after, given the consistent finding of vitamin D deficits in this population, this information is often overlooked or negated [29], despite data that show vitamin D deficits are consistently observed to affect a sizeable proportion of hip fracture cases prior to as well as post surgery [12,30]. As well, results of a recent meta analysis revealing no impact of vitamin D on fracture risk [31] can clearly be confounded by the choice of publications reviewed, the inclusion of studies of dubious quality, the attempted aggregation of diverse measures, variable study durations, fracture type and severity, comorbid status, age, gender, bone status, and vitamin D adequacy definitions, among other potentially confounding variables [15,32,33]. Moreover, optimal intervention approaches are not yet well established, and tend to vary, rather than follow any universal recommendation, while even if vitamin D is delivered as planned in some studies, adherence rates and doses may not be optimal in many cases [34]. On the other hand, the best available evidence shows that calcium and vitamin D supplementation of elderly subjects can decrease the risk of hip and other non-vertebral fractures, especially in institutionalized subjects or elderly subjects with poor calcium and vitamin D status [35]. Moreover, a vitamin D deficiency is often associated with many chronic diseases that can transiently increase fracture risk, especially fragility hip fracture risk in the elderly [36], even if disputed [31]. Graded vitamin D administration has also been successfully applied to reduce pain and falls risk in cases recovering from hip fracture surgery [37].

In this regard, if vitamin D deficits do increase falls and fracture risk, while compromising hip fracture recovery, and are linked to malnutrition, as well as intangible factors, it seems more could be done earlier on to mitigate this possible negative association among vulnerable adults, as well as those aging adults who might be malnourished, or poorly exposed to sunlight on a regular basis. As well, more might be done post surgery by acting proactively [36]. Since both vitamin D injections, as well as taking oral vitamin D supplements as indicated are found to be reasonably safe, perhaps more routine efforts to help those who are deficient to attain an adequate serum and intra cellular vitamin D level, regardless of the lack of definitive research would be helpful. Accordingly, even if serum vitamin D testing is not practical or available [36], and it is the vitamin D metabolic ratio rather than single vitamin D measures that are associated with low bone mineral density and fractures [33], given what we do know, vitamin D administration may yet prove helpful to those presenting for hip fracture surgery and who could be at high risk for low pre as well as post surgical vitamin D levels [3,38], even if vitamin D is not considered an osteoporotic hip fracture determinant [39]. At the same time, this approach may help in fostering overall health, infection protection, while helping to avert excess bone and muscle mass losses along with possible subsequent fractures, as well as the magnitude of bone injury, and post hip fracture surgery survival [30,40-42].

However, to more ably support clinical decisions regarding vitamin D supplementation and others, careful long-term efforts to track its bone building attributes, as well its impact on functional ability and falls and fractures in the post COVID-19 era, where protocols and availability of many key health institutions and services may have been significantly impacted, alongside social support and assistance benefits, among others. Examining the parallel pathways of COVID-19 and hip fracture among the elderly community dwelling adult as this has evolved since December 2019 is likely to be especially revealing and may help to better predict if vitamin D levels warrant careful and proactive attention in the realm of minimizing hip fracture risk and morbidity among this burgeoning and oftentimes frail population.

To this end, examining the validity of one or more of the possible linkages presented in figure 1 may prove highly valuable. The efficacy of tailoring supplementary vitamin D doses for purposes of reducing fragility hip fracture risk, and its disability should also be examined more meticulously in rigorously designed studies in order to rule out competing hypotheses, and to avoid cross sectional inferences that do not take into account the fact that reported vitamin D intake levels may not be the same as actual serum levels, and that its effects may be both disease specific, as well as dose-dependent and take weeks or months to unfold.

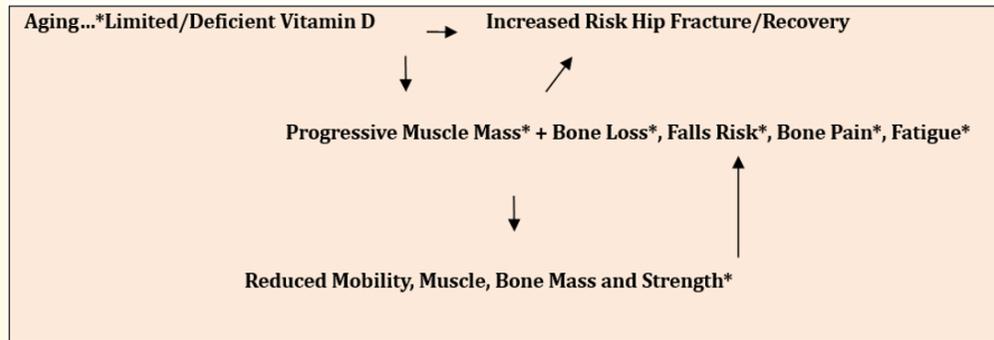


Figure 1: Points* at which vitamin D or a lack thereof may influence the hip fracture risk cycle [4,6,19,32,41,42,45].

In the interim, hip fractures, which clearly produce high levels of mortality and morbidity, must surely remain a major threat to the life quality of many older adults, as well as remaining highly challenging to treat, and prevent. While laudable programs have been undertaken to address this issue, and with some albeit limited success, very little attention appears to have been given in this regard to the probable multidimensional role of vitamin D, as a possible nutrient that might mitigate bone fragility, as well as falls risk and the likelihood of sustaining one or more hip fractures. Its parallel role in averting or mitigating COVID-19 disease, an independent hip fracture correlate, as well as post-surgical inflammation in the presence of a fracture and surgical intervention, and a role for high-dose vitamin D supplementation prior to hip fracture surgery for correcting an appropriately screened and validated deficit as indicated [43,44], also warrants dedicated and timely study.

Conclusion

Based on this current mini-review covering major data sources in peer reviewed journals from January 2020- February 2022, and in agreement with the fact that vitamin D is well known for its diverse actions in promoting bone and musculoskeletal health, and that vitamin D depletion is often noted in those with chronic illnesses such as the elderly who are prone to hip fractures more study in this realm is strongly warranted.

Moreover, even if not a key factor explaining hip fracture risk, a daily intake of vitamin D containing foods in sufficient, but safe amounts, may yet be more helpful than not for minimizing bone resorption processes associated with aging, as well as for fostering bone healing post hip fracture. In the realm of COVID-19 public health imperatives that promote social isolation, closures of health services, lack of staffing in hospitals and nursing homes, ensuring vulnerable adults are able to obtain and maintain an adequate supply and presence of sufficient vitamin D from day to day, may predictably prevent much undue suffering, while favoring more optimal and rapid functional recovery processes in the event of hip fracture surgery, as well as reducing COVID-19 risk, and its highly negative impact on hip fracture outcomes and social costs.

Since time is of the essence, and until more definitive research is forthcoming, and to avert devastating hip fracture outcomes and their multiple physical, social, emotional, and financial repercussions among a vast number of currently frail or at risk for frailty elderly, it appears more concerted proactive actions by practitioners to ensure their patients are able to exhibit sufficient vitamin D levels, especially among those older adults at risk for osteoporosis, would undoubtedly prove helpful. Health providers can be especially helpful in this

regard by carefully screening vulnerable older adults, and directing these older adults and their caretakers accordingly, especially where the patient has brittle bones, or a COVID-19 diagnosis.

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