

Vitamin D and Calcium Abnormalities in the HIV-Infected Population



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KEYWORDS

- Vitamin D • Vitamin D deficiency/insufficiency • Vitamin D supplementation
- Calcium • HIV • AIDS

KEY POINTS

- Vitamin D is involved in several extraskeletal functions.
- Vitamin D deficiency is highly prevalent in the HIV-infected population.
- The adverse outcomes associated with vitamin D deficiency mirror several comorbidities that frequently occur among HIV-infected persons, including osteopenia and osteoporosis, cardiovascular disease, diabetes and the metabolic syndrome, and cancer.
- Studies investigating the effectiveness of vitamin D supplementation in the HIV-infected population are conflicting.
- Standard recommendation regarding screening and treatment of vitamin D deficiency in the HIV-infected population is lacking.

INTRODUCTION

Vitamin D, an essential hormone that maintains normal serum calcium,¹ was shown in the early 1900s to cure and prevent rickets.^{2,3} Osteomalacia has long been recognized as a bone disorder, but it was not until 1967 that vitamin D deficiency was implicated in its cause. More recently, vitamin D has been suggested as a key factor in several extraskeletal functions and disease processes. It has been associated with cardiovascular disease,⁴ diabetes,⁵ muscle weakness and falls,^{6,7} autoimmune disorders,⁸ and certain malignancies including colon, prostate, and breast cancer.^{9–11}

The use of combination antiretroviral therapy (cART) has dramatically reduced HIV-associated morbidity and mortality.¹² Non-AIDS defining illnesses (NADIs; eg, cardiovascular disease, diabetes, osteoporosis, cancer) become more prevalent as HIV-infected individuals grow older.¹³ Modification and prevention of risk factors

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associated with these comorbidities are currently active areas of research. Given the suggested role of vitamin D deficiency in many of these chronic illnesses, the impact of vitamin D deficiency in the HIV-infected population is an important topic that is reviewed here.

VITAMIN D METABOLISM

Vitamin D sources include exposure to sunlight, “oily fish,” cod liver oil, shiitake mushrooms, egg yolks, fortified foods, and supplements.^{14–16} Vitamin D from the skin and diet is transported to the liver and metabolized to 25-hydroxyvitamin D (25-OHD), its major circulating form. 25-OHD is then further metabolized in the kidney to form its biologically active metabolite, 1,25-dihydroxyvitamin D (1,25-OHD). 1,25-OHD maintains calcium in the normal range by facilitating absorption of renal calcium and intestinal calcium and phosphorus.¹⁵ Most experts define vitamin D deficiency as serum 25-OHD less than 20 ng/mL, and vitamin D insufficiency as 25-OHD between 21 and 29 ng/mL. Based on the findings that intestinal calcium absorption is maximized at 25-OHD greater than 32 ng/mL, that nadir parathyroid hormone (PTH) is reached at 25-OHD between 30 and 40 ng/mL, and that secondary hyperparathyroidism is seen at 25-OHD less than 32 ng/mL, a 25-OHD level of at least 30 ng/mL is generally accepted as sufficient.¹⁷

EPIDEMIOLOGY OF VITAMIN D DEFICIENCY/INSUFFICIENCY

Vitamin D deficiency is common worldwide, with an estimated 1 billion people with either vitamin D deficiency or insufficiency. In the United States, data from the 2003 to 2006 National Health and Nutrition Examination Survey (NHANES) estimate the prevalence of vitamin D deficiency at 38%, whereas that of either vitamin D insufficiency or deficiency at 79% among adults.¹⁷

Vitamin D deficiency is also highly prevalent in the HIV-infected population. Among 253 cART-naïve subjects in London, 58% were found to be vitamin D-deficient, whereas 13% were severely deficient (25-OHD <10 ng/mL).¹⁸ Using a more stringent definition of vitamin D deficiency (25-OHD <12 ng/mL), Mueller and colleagues¹⁹ demonstrated a 42% prevalence of vitamin D deficiency among 211 cART-naïve participants in the Swiss HIV Cohort Study. Approximately one-fourth of participants on stable cART have 25-OHD less than 10 to 14 ng/mL, as shown by 2 separate observational studies in New York and the Netherlands.^{20,21} Similar to the general population, the prevalence of vitamin D deficiency in these studies was influenced by the season when 25-OHD measurements were obtained.^{18,19}

Despite these high estimates, the prevalence rates of vitamin D deficiency in the HIV-infected and uninfected populations are comparable. The Study to Understand the Natural History of HIV and AIDS in the Era of Effective Therapy (SUN Study) investigators evaluated the vitamin D status of 672 participants compared with age-matched, race-matched, and sex-matched adult subjects from the NHANES. They found modestly lower vitamin D deficiency prevalence among HIV-infected persons (29.7%) compared with controls (38.8%). The same trend was also observed for vitamin D deficiency/insufficiency.²²

FACTORS ASSOCIATED WITH VITAMIN D DEFICIENCY/INSUFFICIENCY

Several HIV-related and non-HIV-related risk factors are associated with vitamin D deficiency (**Box 1**).^{19,22–27} All non-HIV-related factors are similar to those found among HIV-uninfected cohorts with the exception of intravenous drug use (IDU), which has

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