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Vitamin D Deficiency and its Effects on Oral Candidiasis in HIV/AIDS Patients: A Narrative Review

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Abstract

Background: HIV/AIDS is an immunosuppressive condition often accompanied by other health problems, including fungal infections such as oral candidiasis. This infection is caused by Candida albicans, an opportunistic pathogen that commonly affects immunocompromised patients. Vitamin D is a vitamin which plays a key role in immune regulation and mucosal defenses, and deficiency has been linked to increase in opportunistic infection.

Objective: This study aims to review relevant literature to determine the relationship and effect of vitamin D deficiency in HIV/AIDS patients with oral candidiasis. Methods: Research was conducted on PubMed, ScienceDirect, and Google Scholar using predetermined keywords and the results were limited to articles published in 2015-2025.

Discussion: Vitamin D is an important immunomodulator that regulates innate and adaptive immune responses through vitamin D receptor (VDR) signaling in immune cells. Vitamin D deficiency is common in people living with HIV and is associated with increased immune activation, disease progression, and susceptibility to opportunistic infections. Through reviewing relevant literature, findings suggest that adequate vitamin D status may play a protective role against oral candidiasis and other opportunistic infections in HIV.

Conclusion: Existing studies suggest that vitamin D deficiency may be an important factor in the occurrence of oral candidiasis in HIV patients. However, more research is needed to sufficiently establish a significant correlation between the two conditions.

Keywords: HIV; Oral Candidiasis; Vitamin D Deficiency

1. Introduction

Human Immunodeficiency Virus (HIV) is a retrovirus that infects and progressively destroys $CD4^+$ T lymphocytes, leading to impaired immune function [1]. Persistent viral replication and immune depletion increase susceptibility to opportunistic infections and can progress to Acquired Immunodeficiency Syndrome (AIDS) if untreated. A significant global health issue for individuals living with HIV is vitamin D deficiency [2]. It is linked to an increased risk of chronic infections [1] and oral health problems in HIV patients [3].

Globally, the prevalence of vitamin D deficiency in HIV-positive populations vary greatly. In the United States, Hidron et al. reported that 53.2% of HIV patients were deficient in vitamin D [4]. A study in Romania found that 84.04% of HIV patients were suffering from the condition [5], while in Brazil, 83.4% of HIV patients were diagnosed with vitamin D deficiency [6]. Although the numbers vary greatly by country, they highlight a major hurdle in the management and recovery of quality of life among HIV/AIDS patients.

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This article aims to explore the relationship between vitamin D deficiency and oral candidiasis in patients living with HIV/AIDS by reviewing relevant and contemporary literature in the subject.

2. Material and methods

Comprehensive research was performed using PubMed, ScienceDirect, and Google Scholar databases by applying a Boolean operator–based search strategy to identify relevant publications. The search keywords included "Vitamin D Deficiency", "HIV-Infected" or "HIV-positive", and "Oral Candidiasis". The literature search was carried out between October and December 2025, focusing on English-language articles published within the last ten years. The inclusion criteria for this literature review were: (a) studies related to the topic, (b) original research articles, and (c) publications released between 2015 and 2025. In addition to the inclusion criteria, several exclusion criteria were also applied, including: (a) any article published before 2015 (b) any article published in a language other than English (c) the article should not be a systematic or literature review.

The results were then compiled and presented in a narrative manner, summarized according to keywords and relevant topics.

3. Results and discussion

3.1. Vitamin D and Immune Regulation

Vitamin D plays an important role in regulating the innate and adaptive immune systems through interaction with vitamin D receptors (VDR) [5], which are widely expressed in various tissues and immune cells. Most immune cells express VDR and the enzyme CYP27B1 [1], enabling them to convert 25-hydroxyvitamin D into the active form $1,25(OH)_2D$ locally without being affected by systemic negative feedback mechanisms. Vitamin D bound to vitamin D binding protein (DBP) enters cells through the megalin–cubilin receptor, then activates VDR, which functions as a transcription factor through the formation of heterodimers with RXR and binding to the vitamin D response element (VDRE), as well as through non-genomic mechanisms.

Immunologically, vitamin D enhances innate immune responses and suppresses adaptive immunity [7]. In monocytes and macrophages, vitamin D increases the expression of VDR and CYP27B1, stimulates immune cell chemotaxis, and increases the production of antimicrobial peptides such as cathelicidin LL-37 and β-defensin [1]. Additionally, vitamin D reduces the production of proinflammatory cytokines (IL-1β, IL-6, IL-8, TNF-α, RANKL, COX-2), thereby reducing chronic inflammation, including HIV infection [7].

Vitamin D also modulates dendritic cells by inhibiting differentiation and maturation, decreasing MHC II and costimulatory molecules (CD40, CD80, CD86) expression, and suppressing antigen presentation [8]. In T cells, vitamin D inhibits Th1 and Th17 responses by reducing the production of IL-2, IFN-γ, IL-17, and IL-21, while enhancing Th2 responses and the number of anti-inflammatory regulatory T cells (Tregs) through increased IL-10 and FOXP3 activation [7]. In B cells, vitamin D suppresses proliferation, differentiation into plasma cells, and immunoglobulin production, while inducing apoptosis of activated B cells [7].

3.2. Vitamin D and HIV

It has been observed that many people living with HIV have low vitamin D levels [1, 2]. Vitamin D plays a role in defending against HIV infection and related infections [9], and high vitamin D levels are associated with increased natural resistance to HIV infection [10]. Vitamin D reduces the expression of CD4+ surface receptors [9]. This effect is known to reduce HIV infection by up to 95%. High levels of vitamin D increase the expression of vitamin D receptor proteins, which are associated with the expression of several anti-HIV-1 molecules. High receptor protein density and high vitamin D levels can trigger autophagy processes that inhibit HIV-1 replication in a dose-dependent manner. It has been proven that vitamin D deficiency can be associated with more severe inflammation, tissue dysfunction, the development of comorbidities, AIDS progression, and death [6, 11].

3.3. HIV, Vitamin D, and Oral Candidiasis

Skin and oral manifestations are the most common manifestations in the progression from HIV infection to AIDS. Usually, oral manifestations appear before skin manifestations [12]. The prevalence of people with AIDS experiencing HIV oral manifestations is around 70-80% [13]. These oral manifestations can cause various types of pain and ultimately lead to psychological disorders in patients [13]. Several factors that influence oral manifestations in HIV include a CD4

count <200 per cubic mm, viral load, xerostomia (dry mouth), poor oral hygiene, and smoking [12]. Oral candidiasis with pseudomembranous, erythematous, and hyperplastic types are the most common fungal lesions found in HIV-infected patients [14].

In the oral cavity, vitamin D deficiency is associated with gingivitis, periodontitis, and oral candidiasis [15]. In people with HIV, the effects of vitamin D deficiency are seen in an increased incidence of oral candidiasis, oral squamous cell carcinoma, and Kaposi's sarcoma [16].

Vitamin D deficiency alone is considered sufficient to cause oral candidiasis in HIV patients, irrespective of other contributing factors such as xerostomia, denture use, diabetes mellitus, long-term antibiotic use, chemotherapy, radiotherapy, pregnancy, or poor nutrition [17]. This deficiency is associated with increased calprotectin in the circulation and increased oral candidiasis. Calprotectin is an immune-regulating protein complex that modulates the inflammatory response after being released from neutrophils and monocytes/macrophages [18]. Vitamin D can recruit and inhibit neutrophil oxidative function through its effects on calprotectin. As such, Vitamin D deficiency leads to increased calprotectin in the blood, decreased neutrophil function, and an increased risk of opportunistic infections, which then provides an opportunity for oral candidiasis [19].

Studies have demonstrated the link between vitamin D deficiency and increased rate of developing opportunistic infections. Vitamin D deficiency has been correlated to an increased risk of tuberculosis infection and cytomegalovirus in HIV patients [20]. Furthermore, in a study by Tehrani et al. [19], vitamin D deficiency is significantly associated with an increased risk of oral candidiasis. As such, vitamin D supplementation may be beneficial to mitigating the risk of oral candidiasis in HIV patients.

4. Conclusion

Vitamin D plays an important role in human metabolism, including in maintaining calcium and phosphate balance and in maintaining a healthy immune system. Vitamin D deficiency may occur in patients with HIV, influenced by factors such as poor diet, limited sun exposure, chronic inflammation associated with HIV, and the use of strong antiretroviral therapy drugs. Although several studies have indicated that vitamin D may be one of the factors that influence the occurrence of oral candidiasis in HIV patients, further research is required to establish a significant correlation between the two conditions.

Compliance with ethical standards

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Disclosure of Conflict of interest

No conflict of interest to be disclosed

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