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Prevalence of micronutrients deficiencies in a cohort of HIV-positive individuals on ART

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ABSTRACT:

Background: Micronutrients deficiencies are common in HIV-infected individuals and have been associated with increased morbidity and mortality. In this short report, we aimed at evaluating the prevalence of vitamin D, vitamin B12 and folic acid deficiency in individuals attending the Outpatient HIV Clinic of the Garibaldi Nesima Hospital of Catania.

Patients and Methods: In this cross-sectional study, we consecutively enrolled HIV-positive individuals attending the HIV Outpatient Clinic of the Division of Infectious Diseases in Catania, Italy. Micronutrients and other laboratory data were extracted from the medical records.

Results: 299 individuals were included in our analysis, median age was 46 (39-54) years. Median time since HIV diagnosis was 132 (46-228) months. Median CD4+ T-cell count was 568 (414-713) cells/μl, 83% had an undetectable viral load. Hypovitaminosis D was highly prevalent, with 37% of patients having vitamin D levels <20 ng/ml. On the contrary, only 5.4 and 0.7% of subjects had vitamin B12 and folic acid deficiency, respectively.

Conclusions: Vitamin D deficiency is highly prevalent in HIV-positive individuals and requires appropriate screening and supplementation to maintain skeletal health. More research is needed to assess the impact of vitamin D supplementation on the prevention of other non-AIDS-associated comorbidities.

Keywords: cART, Comorbidity, Folic acid, HIV, Vitamin D, Vitamin B12.

INTRODUCTION

Micronutrients deficiencies are common in HIV-infected individuals and have been associated with increased morbidity and mortality[1-8].

Vitamin D is known to be involved not only in calcium homeostasis, but also in innate and adaptive immune responses[9,10]. In the last few years, several studies have evaluated the prevalence of vitamin D deficiency in HIV-positive cohorts, and shown that vitamin D deficiency is highly prevalent in the setting of HIV infection, with up to 80-90% of individuals having low vitamin D levels in some cohorts[11-13]. Some studies have suggested an association between exposure to certain antiretroviral drugs and hypovitaminosis D[14-18]. Of interest, low vitamin D has been associated with increased risk of cardiovascular disease, bone disease and overall mortality in observational studies[19-20]. Vitamin B12 has been implicated in the promotion of humoral responses, while folic acid improves neutrophil phagocytosis and activity[21]. Low levels of vitamin B12 have been described in HIV-positive individuals, whereas data on folic acid deficiency have been less consistent[22-25]. Vitamin B12 deficiency has been related to increased mortality, CD4 T-cell decline, increased zidovudine-associated bone marrow toxicity, and increased peripheral neuropathy and myelopathy[26-32].

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PATIENTS AND METHODS

Study population

In this cross-sectional study, we consecutively enrolled HIV-positive individuals attending the HIV Outpatient Clinic of the Division of Infectious Diseases in Catania, Italy. All participants provided a written informed consent to participate in the study. We extracted the following parameters from medical records: patient demographics, body mass index (BMI), time since HIV diagnosis and initiation of cART, antiretroviral regimen, HCV coinfection, presence of comorbidities, most recent CD4+ T-cell count, plasma HIV RNA, vitamin D, parathyroid hormone (PTH) levels, calcium, phosphorus, vitamin B12, and folic acid levels. Vitamin D deficiency was defined as a value below 20 ng/ml, whereas vitamin B12 and folic acid deficiency were defined as a value below 200 ρg/ml and 2 ng/ml respectively.

Table 1. Demographics and clinical characteristics of the study population

Variable	N=299
Age (years)	46 (39-54)
Risk factors	
IDU	35 (11.7)
Heterosexual	119 (39.8)
Time since HIV diagnosis (months)	132 (46-228)
Current CD4+ T-cell count (cells/µl)	568 (414-713)
HIV viral load <50 copies/ml	249 (83)
Time on cART (months)	120 (47-205)
Current use of PI	130 (43)
Current use of TDF	184 (62)
Current use of raltegravir	42 (14)
BMI	24.3 (22-26.6)
Current smoking	120 (40)
eGFR (ml/min/1.73 m^2)	100 (87-111)
Hepatitis C coinfection	49 (16)
Diabetes mellitus	22 (7.4)
Vitamin D deficiency (<20 ng/ml)	111 (37)
Vitamin D levels (ng/ml)	23.5 (16.6-30)
Vitamin B12 deficiency (<200 ρg/ml)	16 (5.4)
Vitamin B12 levels (ρg/ml)	315 (222-452)
Folic acid deficiency (< 2 ng/ml)	2 (0.7)
Folic acid levels (ng/ml)	3.5 (2.6-5.3)

Data are n. (%) of patients or median (interquartile range). BMI: body mass index; cART: combination antiretroviral therapy; eGFR: estimated glomerular filtration rate; HIV: human immunodeficiency virus; IDU: intravenous drug user; MSM: men having sex with men; PI: protease inhibitor; TDF: tenofovir.

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences version 22.0 (SPSS, Inc., Chicago, IL, USA). For our descriptive analysis, we used N (percentage) for nominal data and median (interquartile range (IQR)) for continuous data, as appropriate. Correlation between variables was assessed using Spearman's test.

RESULTS

The characteristics of the study population are summarized in Table 1. We enrolled 299 individuals. Median age was 46 (39-54) years, most of the subjects (95%) were Caucasian and men (74%).

40% of patients were infected through heterosexual exposure. Median time since HIV diagnosis was 132 (46-228) months. 83% had an undetectable viral load. Median CD4+ T-cell count was 568 (414-713) cells/µl. Median CD4/CD8 T-cell ratio was 0.75 (0.5-1.1). Median time since cART initiation was 120 (47-205) months. 62% of subjects was receiving tenofovir (TDF), 14% raltegravir, 43% a PI-based regimen. 22% of individuals were highly treatment-experienced (sixth line or more). 16% of individuals were coinfected with hepatitis C, the majority of them as a consequence of previous intravenous drug use. The prevalence of diabetes was 7.4%, while the prevalence of hypertension was 18%. Median BMI was 24.3 (22-26.6). Median CKD-EPI value was 100 (87-111) ml/min. The majority of individuals had vitamin B12 levels (315 (222-452) ρg/ml), as well as folic acid values (3.5 (2.6-5.3) ng/ml) within the normal range. Hypovitaminosis D was highly prevalent, with 37% of patients having vitamin D levels <20 ng/ml. Serum calcium and phosphorus levels were within the normal range in all patients. As expected, vitamin D levels were negatively correlated with age (p=0.03), and PTH levels (p<0.001). No significant correlations were found with vitamin B12, folic acid or other viro-immunological parameters.

DISCUSSION

In line with previous reports from our group and others, we found hypovitaminosis D to be highly prevalent in HIV-infected subjects[8,11-13]. On the contrary, only a small fraction of individuals had low vitamin B12 and folic acid levels.

Vitamin D deficiency has been associated not only with bone disease but also with other comorbidities, including cardiovascular disease and diabetes[19-20]. The availability of effective antiretroviral drugs has transformed HIV infection in a chronic disease. As the HIV population is aging, a significant number of individuals is expected to experience osteoporosis and fragility fractures. As recommended by current EACS guidelines[33], vitamin D levels should be assessed in each individual with low bone mineral density and/or fractures, as well as patients with risk factors, such as dark skin, dietary deficiencies, malabsorption, chronic renal disease, and obesity. Individuals on PI- or EFV-based regimen may be at risk of hypovitaminosis D and could benefit from serum vitamin D assessment. For individuals with vitamin D deficiency, oral or parenteral supplementation is recommended, combined with calcium if dietary calcium intake is insufficient[33].

CONCLUSIONS

Vitamin D supplementation is known to favorably impact skeletal health, however more studies are needed to assess whether correcting vitamin D deficiency could have a favorable impact on the prevention of other non-AIDS-associated comorbidities.

CONFLICT OF INTEREST:

The Authors declare that they have no conflict of interests

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