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ORIGINAL RESEARCH

Prevalence and Predictors of Hypovitaminosis D in Ethiopian HIV-Infected Adults

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Background: Hypovitaminosis D is associated with bone fracture and cardiovascular disease in patients receiving antiretroviral therapy. Currently, there are few data on the magnitude of hypovitaminosis D in people living with HIV in Sub-Saharan country. Therefore, the present study determines the magnitude of hypovitaminosis D in people living with HIV and its associated factors in Ethiopia.

Methods: A cross-sectional study was conducted among 171 adult people living with HIV at Debre Berhan Specialized Hospital. Serum vitamin D was measured. Multivariate logistic regression analysis and p-value <0.05 was used to identify the associated factors of hypovitaminosis D.

Results: In the present study, the prevalence of hypovitaminosis D was 129/171 (75.4%), with 11/171 (6.4%) having vitamin D deficiency and 118/171 (69%) having vitamin D insufficiency. Female sex was significantly associated with hypovitaminosis D (AOR: 3.01, 95% CI = 1.381–6.561, P = 0.006).

Conclusion: Our study found a high burden of hypovitaminosis D among adult people living with HIV on antiretroviral therapy. Female sex was associated with hypovitaminosis D.

Keywords: vitamin D, HIV, antiretroviral therapy, Ethiopia

Background

Hypovitaminosis D is a widespread health problem in the general population as well as in people living with HIV (PLHIV). For example, USA-70.3%,[1] New York City-21.2%,[2] South-Central United States – 64%,[3] Spain – 71.6%,[4] and Uganda – 77%.[5]

Hypovitaminosis D status is a known risk factor for bone fracture and low bone mineral density,[6,7] coronary artery disease,[8] atherosclerosis,[9–11] insulin resistance and type-2 diabetes[12] and neurocognitive impairment[13] in people living with HIV. Additionally, hypovitamin D status is also associated with tuberculosis.[14,15]

Possible established risk factors for hypovitaminosis D have been identified in PLHIV individuals. Some of these are common to the general population, whereas others are related to HIV itself. The presence of dark skin,[16] female,[17] old age,[16,17] high body mass index (BMI), black race,[16] winter season[16] and HAART.[18] In particular, Efavirenz treatment has been associated with low vitamin D status.[17,19] Besides, longer duration of ART, CD4 count <200/μL and advanced stages of disease were independently associated with hypovitaminosis D status.[20]

Currently, there are few data on the magnitude of vitamin D status in PLHIV in sub-Saharan Africa. Most studies of vitamin D status with HIV represent populations from developed countries. The treatment disparities combined with differences in demographics, lifestyle, and nutritional status between Ethiopian and

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Western populations, may make this population more susceptible to hypovitaminosis D. Therefore, the present study will determine the magnitude of hypovitaminosis D in HIV patients and its associated factors in Ethiopia.

Methods and Materials

Study Setting and Design

This study was conducted at Debre Berhan Referral Specialized Hospital (DRSH), Debre Berhan, Ethiopia. The area is characterized by two seasonal climate; a dry season (November–May) and a rainy season (June–September), and ambient temperatures vary from 46°F in December to 69°F in May. A laboratory-based cross-sectional study design was employed among adult people living with HIV on ART, and the study period was from January 1 to 30, 2021.

Study Population and Sample

All Adult PLHIV. A convenient sampling technique was used to include a total of 171 adult PLHIV individuals visiting the selected hospital during the data collection period from January 1 to 30, 2021.

Inclusion and Exclusion Criteria

All Adult PLHIV aged ≥18 years old and treated with ART for at least 6 months were included in the study. Study participants with mental health problems, hearing impairments or any other serious health problems and those patients who would not be able to provide the appropriate information and pregnant women were excluded.

Study Variables

Independent Variables

Age, sex, smoking status, alcohol use, physical exercise, CD4 count, duration on HAART, duration of HIV-infection since first diagnosis, anthropometric indicators, use of corticosteroid, multivitamin take, Crhons ds, suns cream use, sun exposure, use of tanning booth, comorbidities, diarrhea in the past 2 week, Rheumatoid arthritis, and HBV/HCV coinfection.

Dependent Variable

Serum vitamin D status.

Operational Definition

Alcoholic beverage drinkers: Individuals were classified as follows: those drinking on average one or more drink(s) daily; those drinking 4 to 6 drinks weekly; those drinking 1 to 3 drinks weekly; and those drinking less than one drink weekly. (One drink is defined as one bottle of beer, one glass of wine or one shot of liquor).

No drinkers: Individuals who are not currently drinking, and have never drunk alcoholic beverages at all.

Adherence rate is measured based on missed doses per month. The percentage of ARV taken is used as a criterion to classify drug adherence (Good is defined as ≥95% of doses taken as prescribed, Fair defined as 85–94% of doses taken, and poor defined as <85% of doses taken).

Other medications: Participants were taking additional medication other than ART.

Comorbidities were defined as medical conditions clinically diagnosed and present at the time of data collection.

Data Collection and Procedure

Participant age, sex, date of the first HIV-sero positive test, last CD4+ cell count, and any viral load determinations were obtained from the participant's hospital card. Questionnaire-driven interviews were performed by a trained nurse at the DRSH HIV clinic. Self-reported personal and familial history of heart fracture, kidney disease, diabetes, and self-reported alcohol and cigarette use were recorded.

First, the questionnaire was written in English and then translated to Amharic language. The questionnaire was retranslated into English by an expert to ensure its consistency. A half day of training was given to two senior nurses and laboratory technologists about the objective, methodology and ethical issues of the study. Two nurses collected data using a structured questionnaire and a checklist, and two laboratory technologists determined serum vitamin D levels. Pretest was done on 5% of the sample to check the validity of the questionnaire and the checklist. In addition, the completeness of the data was checked daily by the principal investigator.

Anthropometric Measurements

Body weight and height were measured. Weight was measured using a Tanita scale; patients were fully dressed, without heavy clothing or shoes, and height was determined without shoes using a portable stadiometer. Weight to the nearest 100 g and height to the nearest 1 mm were measured. Body mass index (BMI) was calculated by dividing weight (kg) by height (m^2).[21]

Blood Sample Collection and Analysis

For determination of serum vitamin D, after overnight fasting, 5 mL venous blood samples were collected by phlebotomy laboratory technologist under aseptic conditions. A serum sample was immediately separated from the collected venous blood after the blood sample clotted and was centrifuged at 1000–2000 g for 10 minutes. The separated serum was transferred to a Nunc tube and kept frozen at −20°C until processed. Then, serum vitamin D was determined using ichroma vitamin D, which is a fluorescence immunoassay for the quantitative determination of total 25(OH) D2/D3 level and reported in ng/mL. Quality control was done. Vitamin D deficiency was defined as a 25(OH) D level of 20 ng/mL or less, insufficiency as 21–29 ng/mL, and sufficiency as 30 ng/mL or more. Hypovitaminosis D was defined as vitamin D insufficiency or deficiency (<30 ng/mL).[22]

Data Processing and Analysis

Data was checked, cleaned, and entered into Epi-data software version 4.2, and then exported to SPSS version 25.0 software for analysis. The results of the descriptive statistics were expressed as frequency and percentage. Univariate logistic regression was performed to examine the association of independent variables with hypovitaminosis D for all study participants using crude odds ratios (ORs) with 95% confidence intervals (CI). Those independent variables with a *p*-value <0.2 in univariate analysis were included in the multivariable logistic regression models. *P*-value <0.05 on multivariable logistic regression was considered as a statistically significant association.

Result

General Characteristics of Study Participants

One hundred and seventy-one adult people living with HIV participated in this study. Out of this, 107/171 (62.6%) were female and 90/171 (52.6%) of the study participants fall in the age group between 31 and 43 years. The duration of HIV since the first diagnosis greater than 7 year is 102/171 (59.6%), years on HAART > 6 years is 124/171 (72.5%). Most of the study participants taking TDF/3TC/DTG-based regimen 110/171 (64.3%) and 131/171 (76.6%) had undetectable viral load. In the present study, we collect independent variables that may contribute to hypovitaminosis D in the body. Accordingly, we found 34/171 (19.9%) of the study participants use suns cream, and 45/171 (26.3%) use of tanning booth (Table 1).

Prevalence of Hypovitaminosis D and Its Associated Factors

The prevalence of hypovitaminosis D was 129/171 (75.4%), with 11/171 (6.4%) having vitamin D deficiency and 118/171 (69%) having vitamin D insufficiency.

In the bivariate logistic regression analysis, female sex, physical exercise, use of sunscreen and use of tanning booth, were significantly associated with hypovitaminosis D ($P < 0.05$). When these variables were entered and analyzed in a multivariate logistic regression, only female sex was significantly associated with hypovitaminosis D (AOR: 3.01, 95% CI = 1.381–6.561, P = 0.006) (Table 2).

Discussion

The present study assesses the prevalence of hypovitaminosis D and its associated factor in PLHIV on ART. In this study, hypovitaminosis D was 75.4%. This finding was similar with the findings of a study conducted in USA-70.3%,[1] Spain-71.6%,[4] Milwaukee-73%,[23] Uganda-77%,[5] Thailand-71.7%[24] and Bangkok-Thailand 70.5%.[17] However, the finding was lower than the results of studies done in India-92.63%[25] and 89.2%,[20] Michigan-95%,[26] and France-86%.[22] On the other hand, the result of the current study was higher than the finding of a study conducted in New York City-21.2%,[2] South-Central United States-64%,[3] Southern Australian-39%,[27] Italy-47%,[28] Latin American and Caribbean-65.7%,[29] Kazakhstan-65.1%,[30] and Tanzania-52.8%.[31] Additionally, the figure is also higher in non-HIV subjects. For example, a study conducted in Kenya 60%,[32] and Cameron 25.8%[33] had hypovitaminosis D. The difference observed here might be due to sample size variation, study population and design, and weathers of the study conducted.

The prevalence of hypovitaminosis D in our study is higher than compared to non-HIV subjects.

In the current study, female sex was significantly associated with hypovitaminosis D. This finding was consistent with other studies.[17] Available data also showed that hypovitaminosis D can occur in young women, including those who are pregnant, with higher risk with advancing age in a woman's lifecycle.[34] One possible reason might be that females have more hypovitaminosis D, which is more because of heavily clades with clothes and limited outdoor

Table 1 General Characteristics of Study Participants at HIV Clinic of DBSH, Debre Berhan, Ethiopia, 2021

Variable	Category	Frequency	Percent
Sex	Male	64	37.4
	Female	107	62.6
Age in years	18–30	47	27.5
	31–43	90	52.6
	>44	34	19.9
Yrs since diagnosis	<7	69	40.4
	>7	102	59.6
Yrs on HAART	<6	47	27.5
	>6	124	72.5
Yrs on current regimen	<2	141	82.5
	>2	30	17.5
Last CD4 count in cells/mm3	<200	32	18.7
	200–500	63	36.8
	>500	76	44.4
Type of ART	TDF/3TC/EFV	14	8.2
	TDF/3TC/LPV/r	8	4.7
	TDF/3TC/ATV/r	39	22.8
	TDF/3TC/DTG	110	64.3
Drug adherence	Good	133	77.8
	Fair	34	19.9
	Poor	4	2.3
Viral load in copies/mL	Undetectable(<50 copies/mL)	131	76.6
	<1000 copies/mL	26	15.2
	≥1000 copies/mL	14	8.2
Variables	Category	Frequency	Percent
BMI	<18	31	18.1
	18–24.9	111	64.9
	25–26.9	25	14.6
	>30	4	2.3
Alcohol drink	No	165	96.5
	Yes	6	3.5

(*Continued*)

Table 1 (Continued).

Variable	Category	Frequency	Percent
Tobacco smoking status	Current smoker	3	1.8
	Previous smoker	2	1.2
	Nonsmoker	166	97.1
Use of corticosteroid	No	169	98.8
	Yes	2	1.2
Multivitamin take	No	164	95.9
	Yes	7	4.1
Crohn's ds, ulcerative colitis	No	169	98.8
	Yes	2	1.2
Suns cream use	No	137	80.1
	Yes	34	19.9
Sun exposure in minutes per day	<5 mi	4	2.3
	5–15 min	3	1.8
	15–30 min	15	8.8
	>30min	149	87.1
Use of tanning booth	No	126	73.7
	Yes	45	26.3
Other medication	No	159	93.0
	Yes	12	7.0
Comorbidities	No	159	93.0
	Yes	12	7.0
Diarrhea in the past 2 week	No	146	85.4
	Yes	25	14.6
Rheumatoid arthritis	No	164	95.9
	Yes	7	4.1
HBV/HCV coinfection	No	171	100
	Yes	0	0

Abbreviations: HAART, highly active antiretroviral therapy; ART, antiretroviral therapy; Yrs, years; BMI, body mass index.

activity and menopause. However, in contrast to this finding, other studies have not found an association of vitamin D to females.[22,28] This discrepancy might be due to demographic difference and most of the study participants in this study were on efavirenz-based regimen.

Our study needs to be interpreted in the light of its limitations. This study is only conducted in only one referral hospital; therefore, data presented here may not be generalizable to all HIV-infected persons in Ethiopia. Additionally, the sample size is also small. Convenient sampling technique brings in bias. Moreover, the study did not include a control group of HIV-uninfected persons which would have provided better insight into the role of HIV infection and antiretroviral drugs on vitamin D levels.

Table 2 Bivariate and Multivariate Logistic Regression Analysis of Vitamin D Deficiency with Independent Variables, Adult HIV Patients at DBSH, Debre Berhan, Ethiopia, 2021

Variables	Category	Vitamin D Deficiency		COR (95% CI)	AOR (95% CI)
		Yes	No		
Sex	Male	40(62.5)	24(37.5)	1	
	Female	89(83.2)	18(16.8)	2.967(1.450–6.071)*	3.01(1.381–6.561)**
Age	18–30	37(80.4)	9(19.6)	1	
	31–43	64(71.1)	26(28.9)	0.599(0.254–1.414)	
	>44	27(79.4)	7(20.6)	0.938(0.311–2.834)	
Physical exercise	No	69(68.3)	32(31.7)	1	
	Yes	60(85.7)	10(14.3)	2.783(1.263–6.130)*	2.609(0.980–6.949)
Alcohol drinking	No	124(75.2)	41(24.8)	1	
	Yes	5(83.3)	1(16.7)	1.653(0.188–14.565)	
Smoking status	Currently	2(66.7)	1(33.3)	1	
	Quitted	2(100.0)	0(0.0)	–	
	Never	125(75.3)	41(24.7)	1.524(0.135–17.250)	
Use of sunscreen	No	98(71.5)	39(28.5)	1	
	Yes	31(91.2)	3(8.8)	4.112(1.188–14.236)*	1.633(0.269–9.905)
Sun exposure	<5 mi	2(50.0)	2(50.0)	1	
	5–15 min	3(100.0)	0(0.0)	–	
	15–30 min	11(73.3)	4(26.7)	2.75(0.284–26.607)	
	>30min	113(75.8)	36(24.2)	3.139(0.427–23.090)	
Used a tanning booth	No	90(71.4)	36(28.6)	1	
	Yes	39(86.7)	6(13.3)	2.6(1.013–6.672)*	0.831(0.221–3.122)

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CD4	<200	11(34.4)	21(65.6)	1	
	200–500	18(28.6)	45(71.4)	1.31(0.526–3.256)	
	>500	13(17.1)	63(82.9)	2.538(0.989–6.516)	
Yrs since diagnosis	<7	58(74.4)	20(25.6)	1	
	>7	71(76.3)	22(23.7)	1.113(0.554–2.236)	
Yrs on HAART	<6	65(74.7)	22(25.3)	1	
	>6	64(76.2)	20(23.8)	1.083(0.539–2.175)	
Current regimen duration	<2	104(77.0)	31(23.0)	1	
	>2	25(69.4)	11(30.6)	0.677(0.300–1.530)	
Regimen	EFV	9(64.3)	5(35.7)	1	
	LPV/r	7(87.5)	1(12.5)	0.257(0.024–2.732)	
	ATV/r	27(69.2)	12(30.8)	0.8(0.221–2.899)	
	DTG	86(78.2)	24(21.8)	0.502(0.154–1.64)	

Notes: *Statistically significant by univariate logistic regression; **Statistically significant by multivariate logistic regression.

Abbreviations: COR, crude odds ratio; AOR, adjusted odds ratio; CI, confidence interval; EFV, efaverinze; LPV/r, ritonavir-boosted lopinavir; ATV/r, ritonavir-boosted atazanavir; DTG, dolultegravir.

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Conclusion

Our study found a high prevalence of hypovitaminosis D among adult PLHIV on ART. Female sex was associated with hypovitaminosis D. A prospective cohort study with long follow-up and large sample size is recommended to pinpoint the prevalence of hypovitaminosis D and its associated factors.

Abbreviations

ART, Anti-Retroviral Therapy; ATV/r, Ritonavir-boosted atazanavir; BMI, Body Mass Index; CD4, Cluster of Differentiation four; DTG, Dolultegravir; DBSH, Debre Berhan Specialized Hospital, EFV, Efavirenz; HAART, Highly Active Anti-Retroviral Therapy; HIV, Human Immune Deficiency Virus; LPV/r, Ritonavir-boosted lopinavir; SPSS, Statistical Package for Social Sciences; PLHIV, People living with HIV.

Data Sharing Statement

The data used to support the findings of this study are included in the article.

Ethical Approval and Consent to Participate

Ethical clearance was obtained from the ethical review committee of College of Health Science Debre Berhan University with institutional research ethics review committee number of (IRB protocol: DBU/CHS/MN/SG12/2020). Collaboration letter for data collection was also obtained from Debre Berhan Referral Hospital. The objective of the study was briefly clarified and explained for each participant, before enrolling any of the eligible study participants. Samples and data were collected after informed consent had been obtained from the study participants. To assure confidentiality, a code number was used instead of the participants' name or identification number. This study was conducted in accordance with the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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