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Research Article

Hypovitaminosis D, Aging, HIV Infection, HAART, and Other Cardiovascular Risk Factors in Patients from Kinshasa, Dr Congo, Central Africa

Mandina Ndona Madone[1], Longo-Mbenza Benjamin[1,2,6]*, Renzaho Andre[3], Lepira Mbompaka François[1], Wumba -di-Mosi Roger[5], Ngatu Roger[4], Apalata Teke Ruphin[2] and Mambueni Thamba Christophe[1]

[1]Department of Internal Medicine, Faculty of Medicine, Kinshasa University, Kinshasa, Democratic Republic of Congo

[2]Department of Internal Medicine, Cardiology and Physiopathology Service, University Clinics in Kinshasa, Faculty of Medicine, University of Kinshasa and Faculty of Health Sciences, Walter Sisulu University, Mthatha, Private Bag XI, Mthatha 5117, Eastern Cape, South Africa

[3]School of Social Sciences and Psychology, Western Sydney University, Australia

[4]International University of Health and Welfare, Japan

[5]Department of Tropical Medicine, Infectious Diseases and Parasitology Service, University Clinics in Kinshasa, Faculty of Medicine, University of Kinshasa, Democratic Republic of Congo

[6]Biostatistics Unit, Lomo Medical Center and Heart of Africa Center of Cardiology, Democratic Republic of Congo

***Corresponding Author:** Longo-Mbenza Benjamin, Department of Internal Medicine, Faculty of Medicine, Kinshasa University, Kinshasa, Democratic Republic of Congo.

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Abstract

Background: Democratic Republic of the Congo (DRC) along other developing countries, is facing Double Burden diseases grouping cardiovascular diseases, diabetes mellitus, epidemiologic transition, obesity, and HIV/AIDS. Despite the abundant of sun, rare data have shown a significant link between Diabetic retinopathy and Hypovitaminosis D in DRC.

However, there is no attention paid on established immune roles and cardiometabolic effects of Hypovitaminosis D among aging HIV status (Positive and Negative) patients in Kinshasa, DRC.

Therefore, the objective of this study sought to demonstrate potential associations between CVD, sociodemographic, risky behaviors, HIV status, ART regimen (Yes and No), and Hypovitaminosis D.

Methods: This comparative cross sectional study measured the concentrations of 25-hydroxyvitamin D [25(OH)D] for patients admitted to 8 representative hospitals from Kinshasa DRC.

Results: Out of 506 patients, 80.2% (n = 406) and 75.9% (n = 384), 83% (n = 420), 66.6% (n = 377), 58.9% (n = 298), and 59.6% (n = 242) presented HIV positive, female sex, obesity, hypertriglyceridemia, physical inactivity, out of 506 patients, 80.2% (n = 406) were HIV positive whose 75.9% (n = 384), 83% (n = 420), 66.2% (n = 337), 56.1% (n = 284), 34.2% (n = 173) and 58.9% (n = 298) presented female sex, obesity, hypertriglyceridemia, physical inactivity, cigarette smoking, and aging ≥ 60 yr, respectively.

The most significant independent of hypovitaminosis D (66.7% n = 337 with Vitamin D < 30 mg/L vs Vitamin D insufficiency = 20 - 29 mg/L, and Vitamin D deficiency < 20 mg/L) were smoking (OR = 2.7; 95% C/1.1 - 6.4; P = 0.029), excessive intake of alcohol (OR = 2.7; 95% C/1.1 - 6.8; P = 0.033), physical inactivity (OR = 4; 95% C/ 1.5 - 6.4 P < 0.0001), renal dysfunction (OR = 2.7; 95% C/ 1.1 - 6.4; P = 0.037), aging (OR = 4.9; 95% C/ 2.5 - 10; P < 0.0001), hypoalbuminemia (OR = 5.7; 95% C/ 2.4 - 13.5; P < 0.0001), and HIV positive on ART (OR = 12.3; 95% 3.6 - 41.8; P < 0.0001).

Conclusion: Hypovitaminosis D is associated with aging, risky lifestyle, double burden of malnutrition (obesity and hypoalbuminemia), classical and new cardiovascular factors, and ART in aging HIV in KINSHASA population, DR Congo.

Keywords: *Vitamin D; HIV Infection; Cardiovascular Risk Factors; Double Burden of Malnutrition; Central Africa*

Introduction

Sub-Saharan Africa (SSA) is known to be carrying the heaviest burden of HIV/AIDS in the world [1,2] and emerging aging (epidemiologic transition), new cardiovascular risks, double burden of malnutrition (nutrition transition) [3]. Despite low prevalence of HIV infection (1.2% in the general population, the Democratic Republic of Congo/DRC, 1.6% in the western capital Kinshasa Capital, and 4.0% in the eastern province of Maniema) [4,5], the management of HIV infection is limited to some degree of poverty ethnic conflicts, wars, malaria, tuberculosis, malnutrition and accessibility or late initiation of antiretroviral therapy (ART).

Vitamin D (VitD) is a fat-soluble steroid synthesized from 7-dehydrocholesterol, a cholesterol precursor. In general, vitD level is high in the SSA region, reaching levels far beyond the acceptable concentration of 30 ng/L (75 nmol/L) [6-9]. Hypovitaminosis D is well established in western countries that are characterized by temperate cold [10-12], whereas the issue of hypovitaminosis D is now reported for SSA [13], a continent that has an abundance of sunlight. Indeed, a number of studies have shown lower vitD levels in populations at-risk such as women wearing veil or headscarf [14], HIV-infected individuals and tuberculosis patients [15]. For instance, a study conducted by Mbuyamba., *et al*. [16] revealed lower 25 (OH) D levels among Congolese male patients. In addition, a recent Congolese study whose participants were diabetic and non-diabetic patients, showed that retinopathy was associated with a low vitD in Congolese patients with type-2 diabetes [17].

Nowadays, hypovitaminosis D has turned to be a global issue in general [16] and in clinical data from DRC in particular estimated 62% - 95% Ilanga., *et al*. [18], Kabengele., *et al*. [19] and Mvitu [20]. This might be explained in secondarily by both reduced number and low intake of food items that are rich in vitD [13]. Furthermore, a number of lifestyle-related factors that reduce cutaneous synthesis of vitD such as age, weight gain or obesity and physical inactivity which leads to reduced exposure to sunlight might primarily cause hypovitaminosis D [13].

Vitamin D deficiency might impact the bone's architecture and functions, and also increase the risk of cardiovascular diseases [21], insulin resistance and type-2 diabetes mellitus [22], immune dysfunctions [23], infections [24] and some cancers [25]. Those events have also been reported to be associated with HIV infection and antiretroviral therapy (ART) [26]. Hypovitaminosis D does influence HIV infection progression, immune reconstitution syndrome and mother-to-child HIV transmission as well [27]. This suggests that a special attention should be paid to individuals who are at high risk of hypovitaminosis D in general and HIV-infected patients in particular.

Objective of the Study

Therefore, the objective of this study was to determine hypovitaminosis D associated with cardiovascular factors, sociodemographic, risky behaviors, absence of HIV infection, presence of HIV infection not on ART, and HIV infection on ART.

Materials and Methods

Study design and sites

This was a descriptive, comparative and analytical cross-sectional study, conducted between 1 October 2015 and 30 November 2017. It was a multicentric study from hospitals in Kinshasa province, DRC.

The study sites were characterized by the following four health levels of patient management with the use of antiretroviral treatment (ART): Community ART station or level 1; Referral health center or level 2; General referral hospital or level 3; University hospital or level 4.

Of the 1,315 ART facilities scattered across DRC, 335 (25.7%) are located in Kinshasa which were eligible for this study. The inclusion criteria for the health settings were as follows:

- Level 2 - 4 health settings that provide ART, defined based on available resources (health center, general referral hospital, university hospital);
- Level 2 - 4 health settings that provide ART for adults.

Of the 335 health settings of the capital Kinshasa, 114 (34%) were not excluded, including maternities, pediatric services and community ART station. 8 health settings were randomly selected by simple random random draw (Centre Hospitalier Boyambi, Hôpital central

de la Police Nationale Congolaise, Centre Bomoi de N'djili, Centre Hospitalier Kimbanguiste, Hôpital Général de Makala, Centre Médical de Kinshasa, Hôpital Général de N'djili, Cliniques Universitaires de Kinshasa).

Study population and sampling

The study population consisted in HIV-infected and non-infected patients taken care in the ART Centers selected for the study that met the following inclusion criteria: age ≥ 15 years, HIV status (positive not on ART, positive on ART and negative); confirmed by a rapid serological test, ART naïve patient, Patient having a medical record that contains information on study variables of interest, Voluntary participation and provision of informed consent.

The criteria for exclusion were as follows: vitamin D supplementation, treatment for osteoporosis, treatment for a kidney condition, severe liver disease, and refusal to participate in the study.

Laboratory data

HIV rapid serological test (Alere Determine™ HIV-1/2, Abbott) was used in all participants to confirm the presence of HIV specific antibodies. Determine test is one of the three HIV-tests used at first-line for HIV/AIDS screening in DRC.

Total 25-OH Vitamin D (D2 and D3) was measured by the ELISA (Enzyme Linked Immunosorbent Assay) method, which is an enzymatic colorimetric assay.

Operational definitions of outcome variables

Aging, marital status, churches and socio-economic status (SES) were the demographic factors. Marital status has been defined by single/non-married and married. SES was respectively defined by the low (unemployed, housewives, state officials) and high (traders, executives, legislators) levels. Participants were belonging to Reveal-charismatic/Muslim churches or to traditional churches (catholic, protestant, Salvation Army and Kimbanguism churches).

Cardiovascular risk factors**:** the following lifestyle-related and biological parameters were considered as cardiovascular risk factors: cigarette smoking, older age, harmful alcohol intake, physical inactivity, overweight/obesity, abdominal obesity, hypertension, type-1 diabetes, renal dysfunction, hypercholesterolemia (total cholesterol), hypertriglyceridemia and hypoalbuminemia.

Advanced age was defined by an age ≥ 60 years. Cigarette smoking was defined as taking 10 or more cigarettes a day for at least 5 years. Harmful alcohol intake was defined as taking 4 or more drinks per day for men and 3 or more drinks for women. Physical activity was defined as the practice of physical activity for at least 30 minutes, three times or more per week; otherwise, it is considered as physical inactivity.

Body mass index (BMI) it was defined as weight (Kg) divided by height (T) squared and was used to categorize participants according to nutritional status: undernutrition for BMI < 18.5 Kg/m^2; ideal weight or normal nutritional status for BMI = 18.5 - 24.9 Kg/m^2; overweight (BMI) = 25 - 29, 9 Kg/m^2 and obesity for BMI ≥ 30 Kg/m^2.

Generalized obesity included individuals who were overweight and obese ones (BMI ≥ 25 Kg/m^2). Regional redistribution of body fat included abdominal obesity, peripheral obesity: abdominal obesity was defined as waist circumference (WC) ≥ 80 cm, the specific threshold of obesity for both sexes of the black population of sub-Saharan Africa; peripheral obesity (a substitute for clinical insulin resistance) was defined as hip circumference (HC) ≥ 97 cm for the Congolese population in general and for untreated and treated HIV-infected Congolese patients. A patient was considered at risk of cardiovascular disease (CVD) if value of the WC/HC ratio was > 0.85 for a woman and > 0.95 for a man.

Hypertension was defined by systolic blood pressure > 140 mmHg and diastolic blood pressure > 90 mmHg. Information related to Diabetes mellitus was obtained from patients' history and medical records. Renal dysfunction was defined by a glomerular filtration rate < 90 ml/min/1.73 m^2 calculated according to MDRD (uncalibrated creatinine). Dyslipidemia included hyperlipidemia (serum total cholesterol ≥ 200 mg/dL or hypertriglyceridemia ≥ 150 mg/dL). Hypoalbuminemia was defined by albuminemia < 3,5 g/L.

VitD status was defined normal or optimal status by a serum level of Vitamin D ≥30 ng/mL. Hypovitaminosis D was defined by a serum level of vitamin D < 30 ng/mL, vitamin D insufficiency for vitamin D = 20 - 29 ng/mL and vitamin D deficiency for vitamin D ≤ 20 ng/mL.

Ethical considerations

Research approval was obtained from the ethics committee of the Kinshasa University School of Public Health (N° ESP/CE/062/2016) on 29 June 2016. All research procedures were undertaken according to the Helsinki. The participation in the study was voluntary, upon provision of a written informed consent form. Additionally, confidentiality of the information obtained from the participants was guaranteed and access to the study data was allowed only to the investigators.

Data analysis

For categorical variables, data were presented as frequencies and proportions (%), whereas mean and standard deviations were used to present continuous variables.

In univariate analysis, Pearson's chi-square test was used to compare proportions between groups for large sample. Student's t-test was used to compare means between 2 groups for normally distributed variables. However, the analysis of variance (ANOVA) was performed to compare means for ≥ 3 groups.

After excluding confounding factors, a multivariable binary logistic regression analysis was performed to identify independent and significant determinant of hypovitaminosis D. A p-value < 0.05 was considered as the threshold of statistical significance. All analysis were performed using the Statistical Package for Social Sciences (SPSS) version 23 for Windows.

Results

General characteristics

In total, 506 persons were examined, including 406 HIV-infected patients and 100 non-infected (comparative group). The mean age of participants was 57.1 ± 18.3 years; the distribution of the proportions of participants by age-group was as follows: 15 - 39 years (18.6%; n = 94), 40 - 59 years (22.5%; n = 114), 60 - 69 years (32.2%; n = 158) and 70 years or older (27.7%; n = 140). The majority of participants were females (75.9%; n = 384/506) vs. 24.1% males (n = 122): sex ratio = 3 Women: 1 Man.

Out of HIV+, 5,6% (n = 23) were not on ART, whereas, 94,4% (n = 383) were on ART.

Proportions and means of general characteristics were compared between HIV+ and HIV- (Table 1). Values of sex and age were comparable (P > 0,05) between HIV+ and HIV-. However, proportions of low SES, married status and traditional churches were significantly (P < 0,0001) higher among HIV+ than HIV- (Table 1).

Variables	All (n = 506)	HIV + (n = 406)	HIV - (n = 100)	P
Sex, % (n)				
Men	24.1 (122)	23.4 (95)	27 (27)	0.451
Women	75.9 (380)	76.6 (311)	73 (73)	
Age, % (n)				
> 60 yrs	58.9 (298)	59.6 (242)	56 (56)	0.512
< 60 yrs	41.1 (208)	40.0 (164)	44 (44)	
SES % (n)				
Low	75.5 (382)	87.2 (354)	28 (28)	< 0.0001
High	24.5 (124)	12.8 (52)	72 (72)	
Marital status, % (n)				
Married	70.2 (355)	79.6 (323)	32 (32)	< 0.0001
None married	29.8 (151)	20.4 (83)	68 (68)	
Churches, % (n)				
Reveal/Muslim	26.9 (136)	32.8 (133)	3 (3)	< 0.0001
Traditional churches	73.1 (370)	73.8 (273)	97 (97)	

Table 1: *Demographic characteristics of the study participants.*

Table 2 summarizes some cardiovascular risk factors in all and according to the HIV status. Patients infected with HIV were more characterized by excessive alcohol intake, cigarette smoking, physical inactivity and overweight/total obesity, hypercholesterolemia (high TC),

hypertriglyceridemia (high TG) than uninfected patients. Among patients infected with HIV, 154 (30,4%) and 169 (33,4) were hypertension (HTA) and diabetes mellitus, respectively.

Variables	All (n = 506)	VIH + (n = 406)	VIH - (n = 100)	P
Alcohol, % (n)				
Yes	33 (167)	36.2 (147)	20 (20)	0.002
No	67 (339)	63.8 (259)	80 (80)	
Cigarette smoking, % (n)				
Yes	34.2 (173)	32.2 (151)	22 (22)	0.004
No	65.8 (333)	62.8 (255)	78 (78)	
Physical inactivity, % (n)				
Inactive	56.1 (284)	59.6 (242)	42 (42)	< 0.001
Active	43.9 (222)	40.4 (164)	58 (58)	
Overweight/total obesity, % (n)				
Yes	83 (420)	95.6 (388)	32 (32)	< 0.0001
No	17 (86)	20.4 (83)	68 (68)	
Hypercholesterolemia, % (n)				
Yes	16.8 (85)	21 (85)	0 (0)	< 0.001
No	83.2 (421)	79 (321)	100 (100)	
Hypertriglyceridemia, % (n)				
Yes	44.1 (223)	55 (223)	0 (0)	< 0.001
No	55.9 (283)	45 (183)	100 (100)	

Table 2: *Cardiovascular characteristics of the study participants.*

Table 3 presents inequal and significant variations of proportions for several cardiovascular risk factors between HIV-, HIV + not on ART and HIV+ on ART. Sex ratio was similar (P > 0.05) across HIV-, HIV+ not on ART and HIV+ on ART. However, the highest proportions of cigarette smoking, excessive alcohol intake, physical inactivity, total obesity, aging, and hypercholesterolemia were reported from HIV+ on ART vs. intermediate and lowest proportions of those cardiovascular risk factors from HIV+ not on ART and HIV-, respectively. Paradoxically, highest, intermediate, and lowest proportions of renal dysfunction, hypertriglyceridemia and hypoalbuminemia were observed in HIV+ not on ART, HIV+ on ART, and HIV-, respectively.

	VIH - % (n)	VIH + Not on ART % (n)	VIH+ on TARV % (n)	P
Independent Variables				
Sex ratio H:F	1:3	1: 4	1:3	0.739
Cigarette smoking	22 (22/100)	26.1 (6/23)	37.9 (145/383)	0.008
Excessive alcohol	20 (20/100)	26.1 (6/23)	36.8 (141/242)	0.005
Physical inactivity	42 (42/100)	47.8 (11/23)	60.3 (231/383)	0.003
Total obesity	35 (35/100)	95.7 (22/23)	93.7 (359/383)	< 0.0001
Renal dysfunction	58 (58/100)	100 (23/23)	82.5 (316/383)	< 0.0001
Aging ≥ 60 Yrs	56 (56/100)	39.1 (9/23)	60.8 (233/383)	0.098
Hypercholesterolemia	0 (0/100)	0 (0/23)	22.2 (85/383)	< 0.0001
Hypertriglyceridemia	0 (0)	73.9 (17)	53.8 (206)	< 0.0001
Hypoalbuminemia	18 (18/100)	47.8 (11/23)	25.6 (98/383)	0.011

Table 3: *Comparisons of proportions of cardiovascular risk factors by HIV and ART.*

Prevalence of hypovitaminosis D in study participants and according to HIV serological status

In the study population, hypovitaminosis D was estimated 66.6% (n = 337/506), while considering the severity of hypovitaminosis D, 54.6% (n = 273/506) participants had vitD deficiency, whereas 12% (n = 64/506) had vitD insufficiency.

Highest, intermediate and lowest proportions of hypovitaminosis D were significantly ($p < 0.0001$) reported in HIV+ not on ART (100% n = 23/23), HIV+ on ART (76.5% n = 64/23) and HIV- (21% n = 21/100), respectively. Furthermore, when considering the HIV serological status of the study participants, a markedly higher prevalence of hypovitaminosis D was observed in the group of HIV infected patients (77.8% n = 316/406), as compared with non-infected patients, the comparison group (21% n = 21/100).

Relationship between cardiovascular risk parameters and hypovitaminosis D

There was a very significant association ($P < 0.05$) between females (69.3% n = 266/384), age ≥ 60 Yrs (76.8% n = 229/298), total obesity (80.2% n = 337/420), peripheral obesity (79.7% n = 184/231), abdominal obesity (74.6% n = 337/452), cigarette smoking (89.6% n = 155/173), excess alcohol (91% n = 152/167), physical inactivity (90.5% n = 257/284), hypertriglyceridemia (88.3% n = 197/223) and hypovitaminosis D in the study population.

Table 4 shows the trend of values of CVD risk factors among HIV-infected patients according to vitD status. VitD deficiency was commoner in younger patients and obese individuals than aging and normal weight. When lipid profile was considered, vitD deficiency was more common in patients with hypercholesterolemia and hypertriglyceridemia than normal cholesterolemia and normal triglyceridemia. Furthermore, vitD deficiency was also more common in patients with higher waist-to-hip ratio (WHR) than patients with normal WHR.

Variables	Normal VitD	VitD insufficiency	VitD deficiency
Age (years)	51.8 ± 19.1	61.4 ± 17.3	39.6 ± 17.1
BMI (Kg/m^2)	24.7 ± 5.2	29.4 ± 5.5	32.1 ± 6.6
WC (cm)	86.8 ± 12.5	96.4 ± 12.6	100.9 ± 13.9
HC (cm)	82.5 ± 23.6	94.2 ± 21.5	81.8 ± 29.8
TC (mg/dL)	157.1 ± 49.1	142.5 ± 53.5	170.2 ± 51.5
TG (mg/dL)	108.4 ± 94.4	166.2 ± 100.1	206.1 ± 116.6
WC/HC ratio	1.2 ± 0.5	1.1 ± 0.5	1.5 ± 0.8

Table 4: *Distribution of cardiovascular risk factors by vitD status.*

The correlation between cardiovascular risk factors and hypovitaminosis D severity where linear (Figure 1), curvilinear U-shape curve (Figure 2) and J-shape curve (Figure 3).

The direction of linear relationship was significant ($P < 0,05$) positive between BMI (Figure 1a), WC (Figure 1b), serum creatinine (Figure 1c), TG (Figure 1d) and hypovitaminosis D severity, whereas, the direction of linear relationship was significant ($P < 0,05$) negative between albuminemia (Figure 1e).

There was a significant ($P < 0,05$) curvilinear U-shape relationship between age (Figure 2a), HC (Figure 2b) and hypovitaminosis D severity. Last, there was a significant and J-shape relationship between WHR (Figure 3a), TC (Figure 3b) and hypovitaminosis D severity.

Table 5 shows the cardiovascular risk factors independently associated with hypovitaminosis D in the study population. After adjusting for confounding factors (variables univariately associated with hypovitaminosis D: sex, SES, marital status, overweight/total obesity, peripheral obesity, abdominal obesity, hypercholesterolemia, hypertriglyceridemia), the most important independent and significant determinant of hypovitaminosis D were HIV+ on ART, physical inactivity, aging, hypoalbuminemia, renal dysfunction smoking, and excessive alcohol intake.

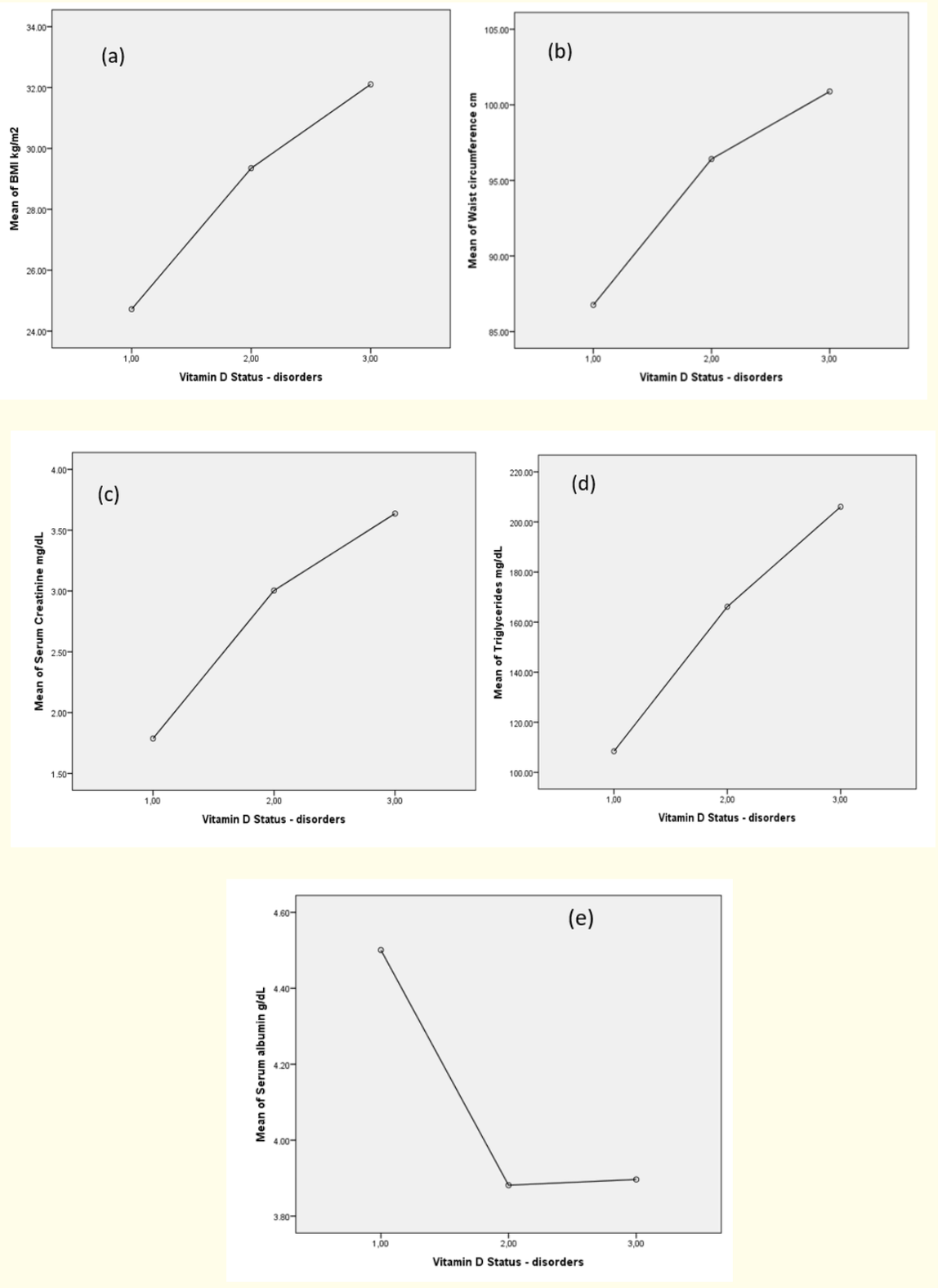

Figure 1: *Relationship between age, BMI, WC, creatininemia, albuminemia and TG with the severity of vitD status.*

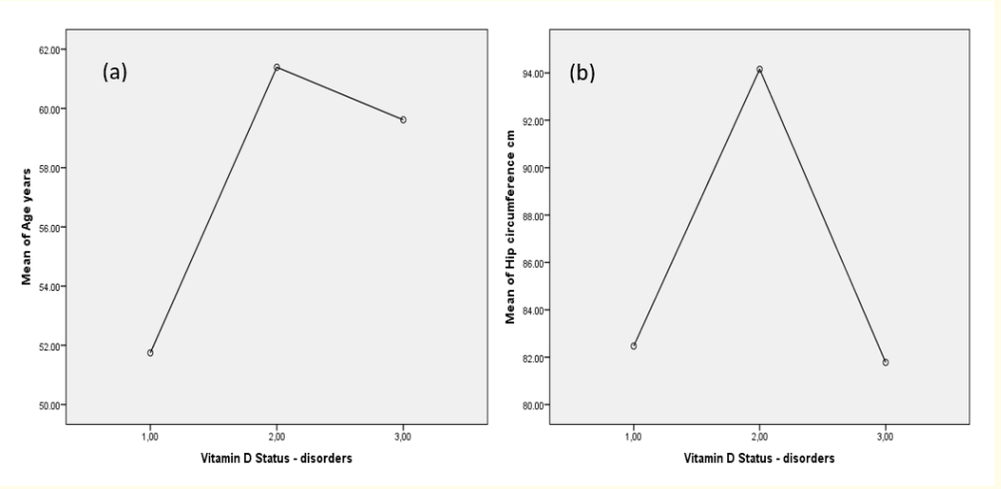

Figure 2: *Relationship between age, and HC with the severity of vitD status.*

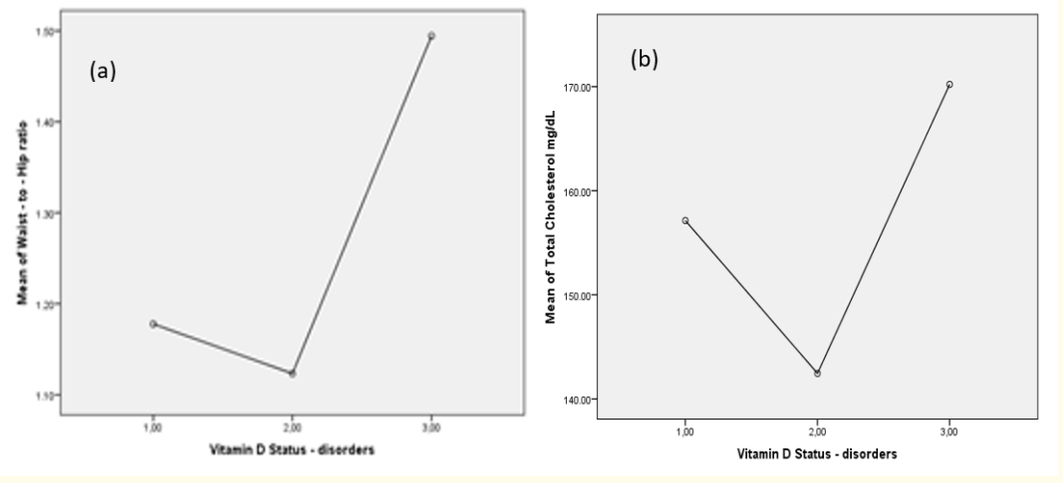

Figure 3: *Relationship between WC/HC and total cholesterol with the severity of vitD status.*

Discussion

This study sought to demonstrate potential (univariate) and independents (multivariate) associations between the cardiovascular factors and variations of vitamin D concentrations as well and hypovitaminosis D status/severity among patients managed for HIV infection and for absence of HIV infection (comparative group) in Kinshasa province, DRC, Central Africa.

The rate of hypovitaminosis D was epidemic closed to 70% in this study and also within the interval of 5 - 90% in the general population from Middle East Africa, North Africa and Sahel regions [14], hypovitaminosis D is also widespread in Middle Eastern countries, probably because of heavy dress habits [14]. Furthermore, the average of hypovitaminosis D rate was high in the present study (66,6%), 62,1% Ilanga., *et al*. [18], and 95,2% Kabengele., *et al*. [19] from Kinshasa Hospital studies. Mvitu., *et al*. with hypovitaminosis D closed to 90% [20] and M'buyamba-Kabangu., *et al*. with high level of reduced vitamin D concentrations [16] reported published data from community/general population and hospitals Kinshasa. The present study, Kinshasa published study [16-20] and the literature [14] confirmed that did vary according to geotype (geographic origins) and to latitude and seasons.

	Beta Coefficient	Standard Error	Wald Chi-square	Adj OR (95% CI)	P-Value
Determinants independents					
Cigarette smoking Yes No	0.977	0.446	4.790	2.656 (1.10 - 6.37) Reference 1	0.029
Excessive alcohol **Yes** No	1.002	0.470	4.550	2.724 (1.08 - 6.84) Reference 1	0,033
Physical Inactivity Yes No	3.708	0.482	59.121	40.752 (15.8 - 104.8) Reference 1	< 0.0001
Renal Dysfunction Yes No	0.811	0.388	4.357	2.249 (1.05 - 4.81) Reference 1	0.037
Aging Yes No	1.601	0.356	20.171	4.958 (2.46 - 9.97) Reference 1	< 0.0001
Albuminemia Low High	1.752	0.437	16.089	5.764 (2.44 - 13.56) Reference 1	< 0.0001
Therapeutic Modalities VIH+ on ART Others	4.814	0.624	59.581	123.18 (36.2 - 418.2) Reference 1	< 0.0001
Constant	-7.025	0.810	75.263	0.001	< 0.0001

Table 5: *Independent association of certain cardiovascular risk factors, therapeutic modalities, and hypovitaminosis D in the study population.*

Out of all HIV-infected patients (not on ART and on ART) in this study, 83% had hypovitaminosis D, whereas only 21% of hypovitaminosis D was reported in the comparative HIV- group, high frequencies comparable to previously published data among HIV+ but HIV- from the literature. However, few published data did not reported significant association between HIV infection and hypovitaminosis D.

For data from only HIV infected persons worldwide, the proportions of hypovitaminosis D reported similar by this study and Mansueto., *et al*. in the range 70.3% to 83.7% [13]. In Sub-Saharan Africa some studies reported lower frequencies of hypovitaminosis D than those reported by the present Kinshasa study and most European and US studies. Thus, the prevalence of hypovitaminosis D varies from 35% to 75% in most studies in warmer tropical Africa in HIV-infected adults [13] in comparison that prevalence of hypovitaminosis D from colder tempered European and North America.

Despite overrepresentation of 3 females vs. 1 male in all participants (HIV+ and HIV-), female sex was not associated with HIV infection but univariately associated with hypovitaminosis D. Hypovitaminosis D, a condition of immune function decline [27], psychological stress, intimate violence, might explain female overrepresentation in this study. Additionally, to female sex the rest of cardiovascular risk factors such as: aging, total obesity, peripheral obesity, and abdominal obesity, cigarette smoking, excess alcohol, physical inactivity, hypertriglyceridemia where potential factors associated with hypovitaminosis D in the present study. The present study confirmed the characteristics of advanced phases of health transitions (epidemiological, demographic and nutritional) [3]. Indeed, urbanisation and health transition favour life style change (cigarette smoking excess alcohol, physical inactivity), hypertension, diabetes mellitus, total adiposity, abdominal

obesity, peripheral obesity, hypercholesterolemia and hypertriglyceridemia are now associated with the emergence of cardiovascular disease in both the DRC and other Sub-Saharan African settings.

In this study, HIV-infected patients were more characterized by total obesity, peripheral, and abdominal obesity, another similar phenomenon also found by Crum-Cianflone., *et al*. in the United States, with 63% of overweight/obese HIV infected patients; Tønnesen., *et al*, Shea., *et al*. showed a significant association between total obesity, abdominal obesity and hypovitaminosis D whereas, pre HAART (Highly Active Antiretroviral therapy) era highlighted dramatic wasting syndrome/cachexia in Sub Saharan African HIV patients. In this study, weight gain among people with HIV is not only due to ART/lipohypertrophy and other factors such as voluntary weight taking for fear of HIV stigma, physical inactivity and advanced age that frequently characterize these patients.

As reported by this study, hypertriglyceridemia and hypercholesterolemia were also associated with hypovitaminosis D in the Kavarić., *et al*. study. Generally, it is recognized that dyslipidaemia is associated with hypovitaminosis D, and one of the mechanisms by which vitamin D can influence cardiovascular risk is that effect on lipids.

Paradoxically, the most important independent and significant determinant of hypovitaminosis D were HIV+ on ART, physical inactivity, aging, hypoalbuminemia, renal dysfunction, cigarette smoking, and excessive alcohol intake in the present Study as well reported by literature.

The association between HIV+ on ART with hypovitaminosis D as reported by some studies.

HIV disease can be accompanied by a reduction in physical activity at the advanced clinical stage of the disease. Tonnesen., *et al*. study carried out in Danmark, involving 738 young adults, showed that physical inactivity was a risk factor for vitamin D deficiency; both physical inactivity and hypovitaminosis D associated with immunity decline [27] and immuno-nutrition disorders, lack of exposure to sun [10]. Indeed, other authors suggest that practice physical activity outdoors is often exposed to solar radiation UVB, source of vitamin D. Furthermore, it was shown that practiced physical activity inside (sun-sheltered) had high vitamin D levels, suggesting that is the concentration of vitamin D during exercise does not depend solely on solar exposure. Some authors suggested that physical activity could stimulate calcitonin secretion, even is responsible for increased calcium absorption and circulating vitamin D levels in circulation after physical activity, which could contribute at maintaining or increasing bone mineral density.

The present study population was generally characterized by a progression of age/aging. This reality is also generally observed in other countries, particularly in the countries of Europe and North America, where the life expectancy of HIV-infected patients has increased by about 10 years since the introduction of HAART in 1996: men reaching age of 73 years and women reaching age of 76 years. Aging was identified as an independent determinant of hypovitaminosis D in the study confirming different results from the literature. Aging was identified as an independent predictor of hypovitaminosis D among HIV-Infected adults living in the Tropics, and among in black and white older adults living in the USA. Indeed, the concentration of 7-dehydrocholesterol from deepest layers of epiderm (skin) do decrease almost with aging. Institutionalized elderly persons (aging), not exposure to sun, are also at high risk of hypovitaminosis D. Recent studies have reported that aging is a significant risk factor of oxidative stress and vitamin D deficiency is also a condition of oxidative stress.

A significant multivariate association between hypoalbuminemia and hypovitaminosis D was demonstrated in the present study, evidence shown also by others authors. Different mechanisms might explain the pathophysiology of hypovitaminosis D to some degree. Serum albumin, defining nutritional status, its decline (hypoalbuminemia) is correlated with low intake of nutrients rich in vitamin D. Further, hypoalbuminemia might be associated with reduced capacity at transporting vitamin D which is circulating under a form linked with "Vitamin D Binding Protein". Another explanation might be a disorder most favouring both hypoalbuminemia and hypovitaminosis D. Hypoalbuminemia is a chronic inflammatory state usually reported in HIV infection persons, reduced exposure to UVB radiation, nephrotic syndrome determining huge loss of urinary proteins (albuminuria) containing also vitamin D binding protein.

Renal dysfunction was among most robust independent determinant of hypovitaminosis D in the present study as reported by different studies with chronic kidney disease (CKD). Among HIV infected persons, CKD is also associated by HIV infection itself, some coinfections, and ART. Many factors have been implicated in the high prevalence of hypovitaminosis D among CKD patients. Patients with CKD, especially on hemodialysis, are likely to have less sunlight exposure. Nutritional factors may also contribute to suboptimal VitD status in

CKD. Patients with CKD frequently have low food intake due to numerous reasons such as reduced appetite, uremic-related gastrointestinal symptoms and dietary restrictions. A low calcium diet can also lead to low 25 (OH)D levels as the secondarily elevated parathormone (PTH) levels will cause a rapid degradation of 25 (OH)D to inactive metabolites. Secondary hyperparathyroidism worsens 25 (OH)D deficiency by promoting the activity of 24, 25-dihydroxylase enzyme and increasing degradation of 25 (OH)D. Proteinuria has also been described as a contributing factor in the pathogenesis of vitamin D deficiency.

Some authors revealed an association between smoking and hypovitaminosis D. Tobacco increases bone resorption and affects bone mass by some changes in sexual hormones metabolism, and significant alterations on the vitamin D-PTH.

Excessive alcohol intake was also identified an important factor associated with hypovitaminosis D in the present study and others literature information. However, the effect of chronic alcohol use on hypovitaminosis D onset is not yet well elicited. A possible explanation comes from alcohol that does interfere not only with the absorption of vitamin D and might be a condition of hypovitaminosis D related to oxidative stress. Ethanol metabolism is directly involved in the production of reactive oxygen species (ROS), a micro-environment conducive to the production of those species such as hypoxia, endotoxemia and cytokines release.

Hypovitaminosis D severity and cardiovascular risk factors

The present study demonstrates opposite direction of relationships between optimal vitamin D status, vitamin D insufficiency, vitamin D deficiency and some traditional cardiovascular risk factors. As expected, the present study revealed significant increase in BMI, WC, creatininemia, triglyceridemia with decrease in vitamin D concentration till vitamin D deficiency. In this study, serum albumin levels decreased with declining vitamin D concentrations till vitamin D deficiency. However, there was a quadratic (curvilinear) relationships between age, HC, WHC, TC and declining vitamin D concentrations: highest, intermediate, and lowest levels of ages and HC being in vitamin D insufficiency, vitamin D deficiency, and optimal vitamin D level, respectively; highest, intermediate and lowest of WHC and TC being in vitamin D deficiency, optimal vitamin D level and vitamin D insufficiency respectively.

Implications on Public Health and Research

The present findings will be used for significance in terms of prevention, early assessment and supplement of Vitamin D among elderly patients with and without HIV infection across Kinshasa Hospitals, DR Congo, Central Africa.

Health promotion and research programmes are recommended in all patients with high risk of HIV infection and cardiovascular diseases in Central Africa.

Limitations and Strengths

The present study was limited for some degreed because its comparative nature without times information. This nature did not establish causality for the relation of cause and effect. The measures of vitamin D might not be precise as their measures were not repeated in this study.

This hospital study does not generalize the rates of hypovitaminosis D, HIV infection, and cardiovascular factors in Congolese general population.

However, the present study had the merit to obtain the first evaluation of epidemic levels of hypovitaminosis D and cardiovascular factors among a large size of HIV patients not only in DRC, and also among persons with black skin in else countries.

Conclusion

The burden and severity of Hypovitaminoses D are highlighted among Congolese patients in Kinshasa, DRC.

Hypovitaminosis D is associated with aging, risky life style, double burden of malnutrition (obesity and hypoalbuminemia), classical and new cardiovascular factors, and ART in aging HIV in KINSHASA population, DR Congo.

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