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BLACK SKIN LIGHTENING USAGE AND DURATION, HIV STATUS, HAART, AND HYPOVITAMINOSIS IN KINSHASA HOSPITALS, DR CONGO (CENTRAL AFRICA)

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ABSTRACT

Background: The artificial lightening of the skin is a social phenomenon in sub-Saharan Africa, most practiced by women using hydroquinone products, topical corticosteroids and mercury. Vitamin D is synthesized in the skin and represents the main source of the body. The use of these lighteners that determine specific skin lesions is therefore likely to cause hypovitaminosis D. HIV infection and its treatment are also a recognized risk factor for hypovitaminosis D.

Objective: This study aimed to evaluate the influence of the use and duration of lightening cosmetics, skin lesions, demographics factors, HIV status, and HAART on vitamin D concentrations.

Design: The plasma level of 25-hydroxyvitamin D [25(OH)D] (25 [OH]D < 30 ng / L= hypovitaminosis D) was measured in a cross-sectional approach, and the use and duration of use of lightening cosmetics, as well as some socio-demographic, therapeutic, and biological variables were collected from HIV infected patients and non-HIV patients in 8 hospitals from Kinshasa province, DR CONGO (DRC).

Results: 506 participants (80.2% n = 406 HIV+ and 19.8% n = 100 HIV-), were examined with 66.7% (n= 337) of hypovitaminosis D. Hypovitaminosis D was estimated 21% in HIV-, 100% in HIV+ not on HAART, and 76,5% in HIV+ not on HAART. 76.1% (n = 385) of the study population used lightening cosmetics whose 47.6% were for more than 5 years. Hypovitaminosis D was more frequent (P <0.0001) among users of lightening cosmetics (73.3% n = 297/405) than among none users of lightening cosmetics (39.6% n = 40/101). There was a very significant positive and linear association with biological gradient (P <0.0001) between increasing duration of use of cosmetics and hypovitaminosis D (39,6% in none users, 58% in 1-4 year-duration of use, 77,4% in 5-9 year-duration of use and 86,4% in ≥ 10 year-duration of use). In logistic regression, cosmetics use (OR = 3.3 95% CI 1.9-5.7, p <0.0001), advanced age (OR = 4.4 95% CI 2.7-7.2; p <0.0001), low socioeconomic status (OR = 2.2 95% CI 1.2-4, p <0.009), and HIV+ on HAART were identified significant and independent determinants of hypovitaminosis D.

Conclusions: The proportions of hypovitaminosis D and use of lightening cosmetics are epidemic in urban Congolese patients in general. The most important determinants of hypovitaminosis D were aging, lightening cosmetics, EFV and ZDV use and lower socio-economic status in these central Africans.

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KEYWORDS : Vitamin D, HIV Infection, Lightening Cosmetics, Aging, EFV, ZDV Kinshasa, Central Africa.

INTRODUCTION

The involvement of the skin in the metabolism of vitamin D is well established. Indeed, the endogenous synthesis of vitamin D takes place at the level of the skin from 7-dehydrocholesterol present in the membranes of the cells of the dermis and the epidermis, under the effect of the energy provided by ultraviolet B (UVB) (1, 2).

The endogenous supply of vitamin D is more important than the exogenous supply of vitamin D (1, 2). The main factors influencing this endogenous production are the seasons, the time of day, latitude, skin phototype, sun exposure duration, type of clothing and the use of sunscreens (3). It is also known that a higher pigmentation of the skin reduces the endogenous synthesis of vitamin D because melanin constitutes a natural sunscreen (4). Not only, its major role in the growth and mineralization of bone, vitamin D has also numerous extra-bone effects on immunity (5), infections (6), cardiovascular risk (7, 8), renal damage (9, 10) and some cancers (11, 12).

Hypovitaminosis D is now reported more among HIV infected patients than among not infected people (13, 14). A general review of hypovitaminosis D in HIV infection, reports high rates of prevalence of hypovitaminosis D between 70.3% and 83.7% (15).

The artificial lightening of black skin is a social phenomenon in sub-Saharan Africa (SSA), and among immigrant populations in Europe or the United States of America (16). This phenomenon, called "Xessal" in Senegal, "Tcha" in Mali, "Tshoko" in the DRC, emerged after African independences in the 1960 (17). Prevalence rates of artificial lightening of skin vary from 25% to 67% in sub-Saharan Africa (17). This skin lightening is more practiced by women using hydroquinone-based pharmacological components, dermocorticoids and mercury (16-18). The median duration of the use of lightening cosmetics is 4 years in Senegal (18). The skin lesions are observed after at least 2 years of use lightening cosmetics in Abidjan (19) and Lomé (20).

HIV infection (21), Highly active antiretroviral therapy (HAART) (22, 23), the use of lightening cosmetics (16, 24) and hypovitaminosis D itself (25) induces specific skin lesions (Kaposi's disease, prurigo , chronic herpes simplex for HIV; toxidermia for ARVs, dyschromia, exogenous ochronosis, increased mycosis and bacterial infections for cosmetics, skin cancer, autoimmune skin diseases, photodermatoses and psoriasis for vitamin D deficiency) likely to compromise the penetration of UVB rays and lead to or aggravate a hypovitaminosis D. However, the epidemiology of the relationship between the use of cosmetics, the duration of use (toxicity) and hypovitaminosis D are not well understood in Kinshasa Hospital. What justifies the initiation of the present study whose objective was to evaluate the influence of the use and duration of lightening cosmetics, skin lesions, demographics factors, HIV status, and HAART on vitamin D concentrations.

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 (26).

Total 25-OH Vitamin D (D2 and D3) was measured by the ELISA (Enzyme Linked Immunosorbent Assay) method, which is an enzymatic colorimetric assay (27).

OPERATIONAL DEFINITIONS OF OUTCOME VARIABLES

Aging, marital status, churches and socio-economic status (SES) were the demographic factors. Advanced age was defined by an age ≥ 60 years. 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 kimbaguisme churches).

The use and the no-use of lightening cosmetics including the steroids, hydroquinone, mercury-based soap and lotions were considered. Skin lesions comprised of hyperchromic spot dermatologic lesions.

VitD status was defined normal or optimal status by a serum level of VitD ≥ 30ng/mL (28). Hypovitaminosis D was defined by a serum level of vitD < 30 ng/mL, vitD insufficiency for vitD = 20–29 ng/mL and vitD deficiency for vitD ≤ 20 ng/mL (29, 30).

ETHICAL CONSIDERATIONS

Research approval was obtained from the ethics committee of the Kinshasa University School of Public Health (No 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) for Windows version 19 (SPSS Inc Chicago, IL,USA).

RESULTS

Table 1. Characteristics of the study participants

Variables	All (n=506)	HIV + (n=406)	HIV – (n=100)	P
Sex, % (n) Men Women	 24,1 (122) 75,9 (380)	 23,4 (95) 76,6 (311)	 *27 (27)* *73 (73)*	0,451
Age, % (n) > 60 yrs < 60 yrs	 58,9 (298) 41,1 (208)	 59,6 (242) 40,0 (164)	 56 (56) 44 (44)	0,512
SES % (n) Low High	 75,5 (382) 24,5 (124)	 87,2 (354) 12,8 (52)	 28 (28) 72 (72)	< 0,0001
Marital status, % (n) Married None married	 70,2 (355) 29,8 (151)	 79,6 (323) 20,4 (83)	 32 (32) 68 (68)	< 0,0001
Churches, % (n) Reveal/Muslim Traditional churches	 26,9 (136) 73,1 (370)	 32,8 (133) 73,8 (273)	 3 (3) 97 (97)	< 0,0001

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 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 was female, 75.9% (384/506) (vs. 24.1% for males); the sex ratio between women and men was 3:1.

Out of HIV+, 5,6 % n=23 were not on ART. Whereas, 94,3% (n=383) were on ART (51,4% n=197 on ZDV+3TC+NVP, 40,2% n=154 on TDF+3TC+EFV, 4,4% n=17 on ZDV+3TC+EFV, 2,3% n=9 on TDF+3TC+NVP, 0,8% n= 3 on TDF+3TC+LPV/r, 0,52% n=2 on ZDV+3TC+LPV/r, and 0,3% n=1 on ABC+DDI+LPV/r)

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

PREVALENCE OF HYPOVITAMINOSIS D, VITAMIN D INSUFFICIENCY, AND DEFICIENCY

The overall prevalence of hypovitaminosis D was estimated 66.6 % (n=337/506). Out of patients with hypovitaminosis D, 54.6% (n= 273) had vitD deficiency, and 12% (n=64) had vitD insufficiency.

FREQUENCY OF USE OF ARTIFICIAL LIGHTENING OF THE SKIN

More than three-quarters of participants (76.1% n = 385) used lightening cosmetics. Figure 1 characterizes the study population by use and stratified duration of lightening cosmetics with 23.9%, 28.5 %, 25.7% and 21.9% respectively without use, use for 1-4 years, 5-9 years, and ≥ 10 years.

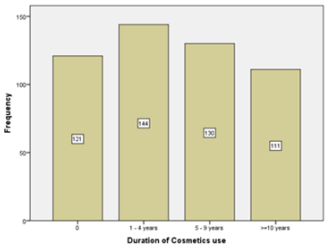

Figure 1. Use and stratified duration of lightening cosmetics in the study population.

UNIVARIATE ASSOCIATION BETWEEN DEMOGRAPHICS FACTORS AND HIV INFECTION, AND HYPOVITAMINOSIS D

There was univariate association between females, aging, reveal/Muslim church, married status, low SES, HIV infection and hypovitaminosis D.

Table 2. Association between demographics factors, HIV infection, and hypovitaminosis D

Variables	Hypovitaminosis D % (n)	OR (95% IC)	P
Sex	69,3 (266/384)	1,6 (1,1 - 2,5)	0,024
• Women	58,2 (71/122)	1	
• Men			
Age			<0,0001
• ≥ 60 yrs	76,8%(229/298)	3 (1,9 - 4,9)	
• < 60 yrs	51,9%(108/208)	1	
Churches			<0,0001
• Reveal/Muslim			<0,0001
• Traditional churches	82,4 (112/136) 60,8 (225/370)	3,1 (2,1-4,5) 1	
Marital status			<0,0001
• Married	74,1 (263/355)	3 (2 - 4,4)	<0,0001
• None married	49 (74/151)	1	
SES			
• Low	76,4 (292/382)	5,7 (3,7- 8,8)	
• High	36,3 (45/124)	1	
HIV Status			
• HIV+	77,8 (316/406)	13,2 (7,7-22,6)	
• HIV-	21 (21/100)	1	

UNIVARIATE ASSOCIATIONS BETWEEN THE USE OF LIGHTENING COSMETICS, DERMATOLOGICAL LESIONS AND HYPOVITAMINOSIS D

Hypovitaminosis D was more frequent (P<0.0001) when

lightening cosmetics were used (73.3% n=297/405) than when not used (39.6% n=40/101). In addition, there was a very significant biological gradient (P<0.0001 trend) between increasing the duration of use of cosmetics and hypovitaminosis D in the study population (Figure 2).

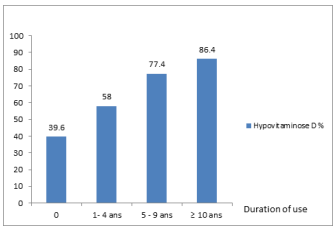

Figure 2. Relationship between the duration of use of lightening cosmetics and hypovitaminosis D in the study population.

There was a positive and very significant association (P <0.0001) between hyperchromic spot dermatologic lesions and hypovitaminosis D: hypovitaminosis D more common in hyperchromic lesions (90% n = 45 / 50) in the absence of dermatological lesions (64% n = 292/456).

The use of cosmetics was more (P<0.001) reported by women (82.3% n=299/355, P=0.038) than by men (68.9% n=84/122). Aging was more associated with the use of cosmetics (83.9% n=250/298, P=0.009) than was the young age (74.5% n=155/208). reported more use of cosmetics (83.6% n=321/384) than did singles (74.8% n=113/151). Cosmetics use was more reported (P<0.0001)) by women of low socioeconomic status (84.3% n=322/382) only by high SES participants (66.9% n=83/124).

INDEPENDENTS DETERMINANTS OF HYPOVITAMINOSIS D

Two multivariable models (logistic regression and multiple linear regression) were used to identify independent determinant of hypovitaminosis D and vitamin D variation in the study population.

After adjusting for confounding factors (marital status and gender) using the binary logistic regression model, cosmetics use, low socioeconomic status, advancing age, ART regimens ZDV + 3TC + NVP, TDF + 3TC + EFV, ZDV + 3TC + EFV, and TDF + 3TC + NVP or LPV / r were identified as independent and significant determinants of hypovitaminosis D in the study population (Table 3).

Table 3. Independent associations between the use of cosmetics, sociodemographic factors, therapeutic modalities and hypovitaminosis D in the study

	B	ES	Wald	Adj OR (95% CI)	P value
independents variables					
Use of cosmetics • Yes • No	1,181	0,247	16,854 Refere nce	3,3 (1,9-5,7) 1	<0,00 01
SES • Low • High	0,787	0,302	6,772 Refere nce	2,2 (1,2-4) 1	0,009
Advancing age • Yes • No	1,483	0,247	36,112 Refere nce	4,4 (2,7-7,2) 1	<0,00 01
ART Regimens • ZDV+3TC+NVP • TDF+3TC+EFV • ZDV+3TC+EFV • TDF+3TC+ NVPou LPV/r	 2,379 2,241 2,001 1,384	 0,364 0,371 0,638 0,713	 42,648 36,570 9,832 3,875	 10,8 (5,3-22) 9,4 (4,6-19,5) 7,4 (2,1-25,8) 4(1,002-16,1)	<0,00 01 <0,00 01 0,02 0,05
Constant	- 3,459	0,420	67,669		<0,00 01

After adjusting for the confounding variables using multiple linear regression model according to the antiretroviral molecules, 13.5% of variation (R2 adjusted) of the decrease in vitamin D concentrations (towards hypovitaminosis D) were predicted (explained) significantly and independent by increased viral load, increased duration of cosmetic use, aging, and female sex (Table 4 and Figure 3).

Table 4. Independent role of viral load, duration of use of cosmetics, age advancement and sex on the prevalence of hypovitaminosis D

independents variables	Coefficients non standardizes		Coefficients Standardizes Beta	P value
	B	ES		
Viral loads (copies/mL)	-3,847	4,36	-0,224	< 0,0001
Duration of cosmetics use (yrs)	-2,235	0.00	-0,146	0,003
Age (yrs)	-0,33	0,75	-0,134	0,006
Female sex	-4,726	0,05	-0,123	0,012
Constant	39,68	1,86		< 0,0001

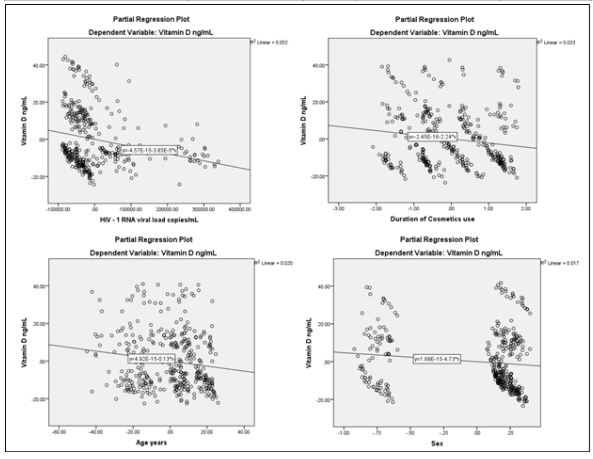

Figure 3. Straight lines and partial regression equations of serum vitamin D concentrations explained by sex, age, viral load and duration of use of cosmetics.

DISCUSSION

This study sought to demonstrate potential associations between the use and duration of lightening cosmetics, skin lesions, demographic factors, HIV status, and HAART on vitamin D concentrations among patients managed for HIV infection and for absence of HIV infection with inflammation (comparative group) in Kinshasa province, DRC, Central Africa.

Hypovitaminosis D varied according to geotype (geographic origins) in this study and in the literature (31, 32). Indeed vitamin D concentrations are impacted by latitude and seasons (3, 33). The rate of hypovitaminosis D was closed to 70% in this study as also as within the interval of 5 - 90% in the general population from Middle East (35), North Africa (34, 35) and Sahel regions (36), hypovitaminosis D is also widespread in Middle Eastern countries, probably because of heavy dress habits (34, 37). Furthermors, the average of hypovitaminosis D rate in Kinshasa megacity, DRC, was high from the present study in Hospital (66,6%), 62,1% Ilanga and al (38), and 95,2% Kabengele and al (39) in Hospital studies. Mvitu and al (40) in both community and the Hospital, and M'buyamba-Kabangu and al (41) in the general population was also reported high frequencies.

Out of HIV-infected patients in this study, 83% had hypovitaminosis D, whereas only 21% of hypovitaminosis D was reported in the comparative group confirming (14, 42) and not confirming (43, 44). Indeed, hypovitaminosis D rates from the present results were similar to those reported in some studies among HIV-infected patients versus the general population (14, 42), while other studies did not find difference between HIV-infected patients versus the general population (43, 44).

The proportion of hypovitaminosis D found in this study among HIV-infected patients was in the range reported by Mansueto et al, in their review of hypovitaminosis D in HIV infection, where almost all of studies did find a high prevalence of hypovitaminosis D ranging from 70.3% to 83.7% in HIV-infected patients worldwide (15). In Sub-Saharan Africa, including the present Kinshasa study reported frequencies appear to be lower than those reported by most European and US studies (15). Thus, the prevalence of hypovitaminosis D varies from 35% to 75% in most studies in warmer tropical Africa in HIV-infected adults (43-45) in comparison studies from colder tempered European (13, 42) and North America (46, 47).

More than 3/4 (76.1%) of the participants in this study used lightening cosmetic products. This proportion was close to that found by Hardwick et al (69%) in South Africa (48), slightly higher than that found by Wone et al (67%) in Senegal (49), but much higher than that of 25 % reported in Mali (18). The risk of toxicity related to the use of corticosteroids, hydroquinone, and the mercury salts contained in these products was estimated to be real in 47.6% of the participants in the present study with a duration of use of more than 5 years, well above the onset of lesions observed after the start of the use of lightening cosmetics (≥ 2 years) in Abidjan (19) and Lomé (20).

As reported in Senegal (49) and Mali (18), female sex, adulthood, being married, low socioeconomic status, were identified as significant contributing factors to the use of cosmetics in this study. In contrast to the data in this study,that from Côte d'Ivoire reports the use of cosmetics for skin depigmentation among young urban women between the ages of 20 years and 30 years, single, educated and professionally active, wanting to be more beautiful (19).

The relationship between the use of cosmetics, the duration of use (toxicity), hyperchromic dermatological lesions and hypovitaminosis D are not yet specifically explained in the literature whereas the results on cosmetics issues in the present study could be explained by several complex physiopathological mechanisms: skin application of hydroquinone / corticosteroid-based products leads to premature aging of the skin with a decrease in the concentration of 7-dehydrocholesterol in the deep layers of the epidermis which reduces the rate of vitamin D (50); exogenous ochronosis (blackish reticulate layers), which is the most typical complication associated with prolonged application of hydroquinone, occurs mainly in exposed photo areas and results from a cumulative photo-toxic reaction leading to the alteration of melanocytes and elastic tissue (24); with the inhibition of melanin production, the skin loses its natural protection against the UVA and UVB rays of the sun and UV light can lead to DNA damage, inflammatory responses, skin cell apoptosis (programmed cell death), skin aging, and skin cancer (50, 51) that may compromise the skin synthesis of vitamin D. Vitamin D deficiency has been associated with skin lesions including skin cancer, autoimmune skin diseases, photodermatoses, atopic dermatitis and psoriasis (52).

This study also showed that the use of cosmetics among elderly HIV patients with a low socio-economic status under antiretroviral therapy with EFV and ZDV were at high risk of hypovitaminosis D. It should be recalled that in sub-Saharan Africa, 60% of HIV infected persons are women (53, 54), most of female users of cosmetics live in precarious situations (55). The advanced age as well as the use of lightening cosmetics are both responsible for an aging of the skin that can explain the hypovitaminosis D. Indeed, the concentration of 7-dehydrocholesterol in the deep layers of the epidermis decreases with age (75% reduction in skin regeneration at age 70 years) (56, 57). In addition, the decrease in vitamin D concentrations was explained by the increase in the duration of use of cosmetics and the advancement in age in the present study, attesting that the appearance of the skin toxicity of these cosmetics is depending on the duration of use (17-19).

IMPLICATIONS FOR PUBLIC HEALTH

The present findings will impact in terms of public health (prevention, education, attitude and practice) about cosmetics use in general population and among HIV infected patients. The present information will be disseminated for information, education, and change of behavior: the proscription of the use of cosmetics, the non-use (primordial prevention) and to stop use (primary prevention) of these products in general, and by HIV patients especially in the elderly, poverty reduction, Improving the management of HIV patients (monitoring the efficacy of treatment and molecules at risk of hypovitaminosis D, prevention and treatment of skin lesions, promoting appropriate diet rich in antioxidants including vitamin D, and vitamin D supplementation) (58).

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 cosmetics use in Congolese general population.

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

CONCLUSION

The extent of hypovitaminosis D and its severity is more marked in HIV infected patients than in non-HIV-infected individuals. The use of cosmetics, the prolongation of cosmetics use , the female sex, aging, the increase in HIV viral load, the reduction of CD4 +, the low socio- economic status, the combination for molecules of EFV and ZDV were the factors associated with hospital hypovitaminosis D in Kinshasa.

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