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Prevalence of Vitamin D Deficiency in Adult Human Immunodeficiency Virus Infected Persons at District Hospital in Nairobi, Kenya.

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Abstract: ***Background:*** *The increased availability of highly active antiretroviral therapy (HAART) for Human immunodeficiency virus (HIV) infected patients has led to significant reduction in mortality. However, there is increasing evidence that stable HIV positive patients on HAART have chronic underlying inflammation. This leads to premature age associated non-Acquired immunodeficiency syndrome (AIDS) related events. Vitamin D deficiency (VDD) in HIV positive patients has been associated with disease progression, chronic non-communicable diseases and increased mortality. Both HIV and HAART have been shown to increase the risk of VDD. Furthermore, supplementation of vitamin D has been shown to reduce HAART related bone mineral density loss by up to 50%.*

Objective: *To determine the prevalence of vitamin D deficiency in adult HIV infected persons at Mbagathi district hospital.*

Design: *Hospital based cross sectional descriptive study.*

Setting: *Comprehensive Care Clinic at Mbagathi district hospital located in Nairobi County.*

Subjects:*128 HIV infected persons who gave consent.*

Results: *68% of the patients were females. The mean age was 41 years. Eight (6.3%) patients were classified as vitamin D deficient25 hydroxyvitamin D (25(OH)D) <20 ng/ml, while thirty-eight (29.7%) had vitamin D insufficiency 25(OH)D 21-29 ng/ml and eighty-two (64%) patients had normal levels25(OH)D 30-100 ng/ml. HAARTnaïve patients were 5.3 times more likely to have VDD. We did not find any associations between vitamin D and age, gender, body mass index (BMI), WHO stage and estimated glomerular filtration rate (eGFR).*

Conclusion: *Prevalence of Vitamin D deficiency was found to be low in our study population*

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I. Introduction

According to World Health Organization (WHO) there were 35 Million people living with HIV worldwide at the end of 2013(1). In Kenya, the prevalence of HIV in adultsat the end of 2013 was 6% and the total number of people living with HIVwas estimated to be 1.6million(2). The dramatic increase in HAART therapyhas led to a marked reduction in AIDS related deaths(2).There is increasing evidence that these stable HIV positive patients havecontinuousunderlying chronic inflammation with chronic immune activationdespite being HAART. This leads to premature age-associated non-AIDS related events including metabolic, cardiovascular, and bone disease.

Prevalence of VDDin HIV positive patients has been reported to be as high as 91% 25(OH)D<30ng/ml in United Kingdom to as low as 6% 25(OH)D <20ng/ml in Italy. Risk factors for VDD in HIV patients can be classified as HIV independent and HIV dependent. HIV dependent factors include, elevated TNF alpha and use of HAART(3).Studies have shown that VDD affects disease progression, skeletal health and extra skeletal health in these patients(4)(5)(6). HIV patients with VDD have a twofold chance of all-cause mortality compared to patients with adequate vitamin D (4)(7). A strong association between VDD and active tuberculosis in HIV patients has been reported(8). This results from the fact that vitamin D is a known immunomodulator. Finally an association between vitamin D deficiency in HIV positive patients and increased risk of cardiovascular disease and diabetes mellitus has been reported in several studies(6)(9).

However, recently studies have been done looking at the effects of vitamin D supplementation on skeletal and non-skeletal health in HIV patients. It is now known that vitamin D supplementation can reduce bone loss by up to 50% in patients on HAART(10). Supplementation has also been shown to reduce risk of type 2 diabetes mellitus in HIV patients(11). Vitamin D deficiency is thus a modifiable factor, it is easily measured in the laboratory and it can easily be treated via supplementation.

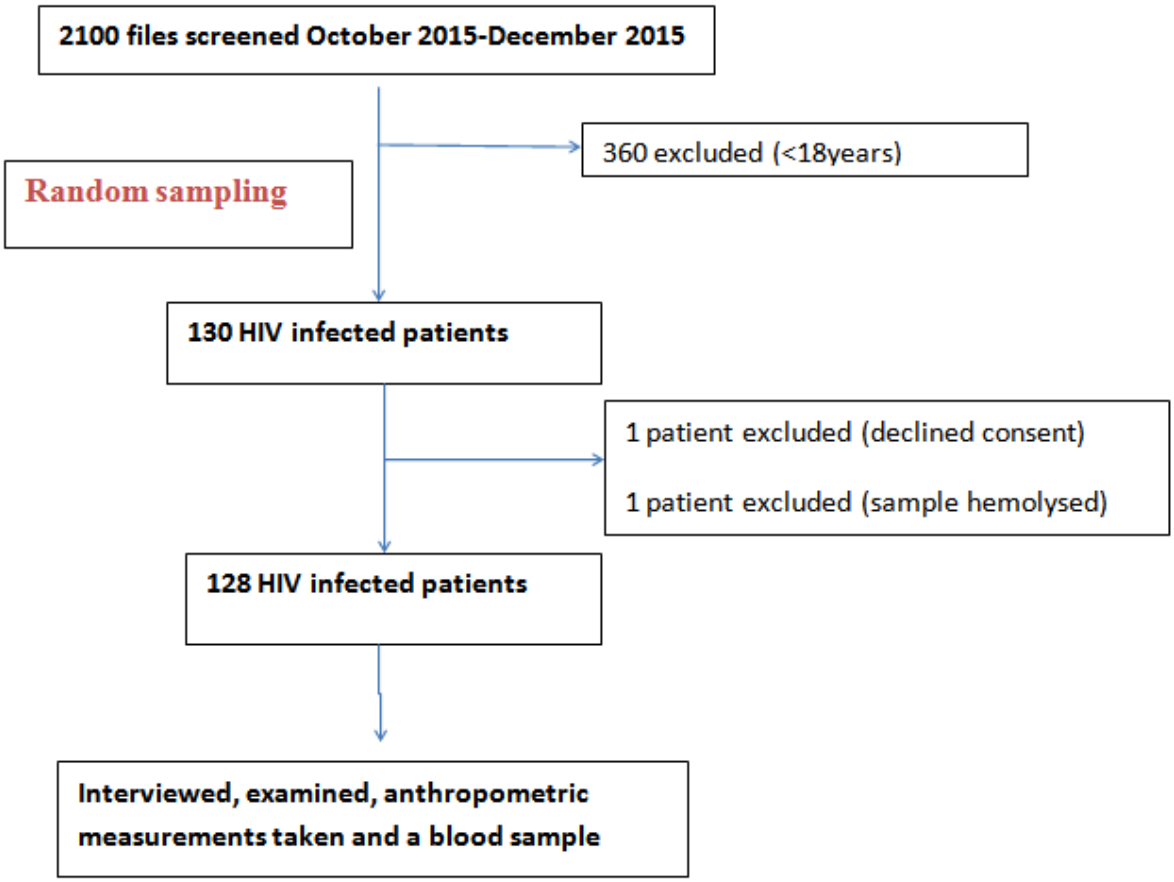
II. Materials And Methods

This was ahospital based descriptivecross-sectional study done between October 2015 and December 2015. The subjects were all HIV infected patients on follow up in Mbagathi District Hospital who gave consent. A through medical history was then obtained and a brief examination done. Blood for serum hydroxyvitamin D and creatinine was then drawn.

Results

Records of 2100 patients reviewed; 360 were excluded as they were aged less than 18 years. Systematic random sampling was done daily to select 5-10 patients per day. A total of 130 patients were recruited between October 2015 and December 2015. 2 patients excluded as 1 declined consent and the second one the sample was hemolysed, a total of 128 patients were analyzed.

Figure 1: Recruitment flow chart



Population Characteristics

Mean age of our population was 41.4 years. Majority of the patients were females at a total of eighty-eight (68.8%) while males were forty (31.2%).

Table 1: Socio-demographic characteristics

Variable	Frequency (%) n=128
Mean age (SD)	41.4 (9.9)
Age in years <20 20-29 30-39 40-49 >=50	 1 (0.8) 14 (10.9) 40 (31.3) 47 (36.7) 26 (20.3)
Gender Male Female	 40 (31.2) 88 (68.8)

Clinical Characteristics

Eighty-five (66.4%) of the patients had been diagnosed as HIV positive for more than six years. One hundred and five of the patients (82%) were onHAART. Most patients (68.6%) were on 1st line treatment. The mean CD4 count was 514 cells/ml.Majority of the patients were betweenWHO stage 2 or 3. The mean BMI was 25.5. Majority of the patients had a preserved renal function with an eGFR of >90 ml/min (table 2). Thirty patients (23.4%) had been treated for tuberculosis, majority having been treated for tuberculosis more than 5 years earlier. Only eleven patients had other co-morbidities which included hypertension, diabetes mellitus and cancer.

Table 2: Clinical characteristics

Variable	Frequency N=128 (%)
Duration since HIV diagnosis <1 year 1-5 years 6-10 years >10 years	 15 (11.7) 28 (21.9) 54 (42.2) 31 (24.2)
On antiretroviral drugs Yes No	 105 (82.0) 23 (18.0)
Current ARV regimens (n=105) TDF+3TC+EFV AZT+3TC+NVP Other	 40 (38.1) 15 (14.3) 50 (47.6)
Median CD4 count (IQR)	514.0 (336.0-680.0)
CD4 levels <200 200-499 >=500 Missing	 15 (11.7) 43 (33.6) 65 (50.8) 5 (3.9)
Mean BMI (SD) **Category, n (%)** Underweight Normal Overweight Obese	25.5 (5.0) 5 (3.9) 63 (49.2) 32 (25.0) 28 (21.9)

Serum 25-Hydroxycholecalciferol

A total of 8 patients (6.3%) were classified as vitamin D deficient while thirty-eight patients (29.7%)had vitamin D insufficiency and eighty-two patients (64%) were classified as normal (table 3). The mean (SD) serum 25(OH)D was 37ng/ml (13.1).

Table 3: Vitamin D deficiency

Variable	Frequency N=128 (%)	95% CI
Serum 25-VD Mean (SD) Median (IQR) Min-Max	 37 (13.1) 36.2 (26.1-47.5) 4.6-66.9	
Serum 25-VD <20 (vitamin D deficiency) 21-29 (vitamin D insufficiency) 30-100 (Normal)	 8 (6.3) 38 (29.7) 82 (64.0)	 2.3-10.2 21.1-37.5 56.3-72.7

Associations Between Variables

HAART naïve patients were 5.3 times more likely to have VDD (P=0.034). However, further exploration was not possible as the number of patients with VDD was too small. We did not find any statistically significant association between VDD and age, gender, body mass index, WHO stage and eGFR. We also attempted to further explore for associations between vitamin D deficiency and insufficiency combined in comparison to normal levels. Female patients were noted to be six times more likely to be vitamin D deficient (P=0.001), no other significant associations were found.

Discussion

The main aim of this study was to determine the prevalence of vitamin D deficiency in adult HIV infected persons attending Mbagathi district hospital.

Using a cutoff of 25 hydroxyvitamin D <20ng/ml to describe VDD, our study population generally had a low prevalence of vitamin D deficiency at 6.3%. The mean serum 25(OH)D levels were 37ng/ml. HAART naïve patients were 5.3 times more likely to have VDD (P=0.03). In our study, we did not find any other significant associations. The low prevalence of VDD could possibly be supported by the fact that this was arelatively young population. Young people are known to synthesize and produce more vitamin D as they have more levels of 7-dehydrocholestrol (3). Holick et al in 2013 did a study to compare the serum vitamin D concentration in young versus elderly people after total body exposure to sunlight. The increase in serum vitamin D concentration in the young population was four times more than that in the elderly population(12). All the eight patients who had VDD were females. Females are known to have a higher risk of VDD as they have a higher body fat content and vitamin D is sequestered in fat(3). Kenya is also a sun rich region with all year-round sunshine as it is near the equator. Countries between $0\text{-}10^0$ latitude have intense sun all year round. Nairobi where the study was done lies 1^0 south. According to the WHO UV index, Nairobi has a UV index between 11-13 and this is classified as extreme sunlight(13). The samples were also taken between October and December which are known to be warm months with a lot of sunshine. Sun facilitated skin synthesis is the main source of vitamin D. Previously all HIV positive patients in Kenya were on multivitamins however currently most clinics are not giving the patients multivitamins routinely. In our study population, none of our patients were on routine multivitamins.

Our results on prevalence of VDD were comparable to other studies done in East Africa. Sudfeld et al in Tanzania found the prevalence of vitamin D deficiency in HIV patients 25(OH)D (<20ng/ml) at 9.2%, insufficiency (21-30ng/ml) at 43.6% and 47.2% had normal vitamin D levels (7).Nansera et al in a study done in Uganda on vitamin D and calcium levels in patients with HIV and TB, vitamin D deficiency(25(OH)D <12ng/ml) was present in 10% of HIV infected subjects, 12% of TB-HIV co-infected and none of the controls (14). Nansera et al used a different methodology for analysis of 25(OH)D with different reference ranges and thus direct comparison of the results may not be possible. We however notice that the prevalence of vitamin D deficiency was low in the HIV patients. These findings would be supported by the fact that in all the three studies the population was young. In Tanzania majority of the patients were between the age of thirty and fifty while in Uganda the mean age of the population was thirty five (7)(14). The three studies were also done in East Africa which is classified by WHO to be a sun rich geographical region. Tanzania and Uganda both have a WHO UV index of 11, which is classified as extreme sunlight (13).

Our findings however did not compare to other local studies done in Kenya. In a recent study done by Gichuhi et al at Aga Khan University hospital in 2015, the prevalence of VDD (25(OH)D <20ng/ml) in HIV patients was 29% for patients on HAART and 49% for HAART naïve patients(15). This was higher than the prevalence in our study. Gichuhi et al used a similar methodology for 25(OH)D analysis and similar reference ranges to our study. Possible explanations for the difference in the results would include the different social demographics between the two populations. Aga Khan University hospital is a private tertiary hospital located in an uptown neighborhood. Patients seen in the hospital are more likely to be of a higher socioeconomic status. These patients are more likely to have white collar jobs which are indoors resulting in reduced sun exposure. In contrast, a study done previously in our study population on bone mineral density by Abdullahi et al showed that 53% of the patients seen in the Mbagathi hospital CCC earn less than Ksh.5000 a day (unpublished data). People from poor socioeconomic background are more likely to do outdoor casual jobs with adequate sun exposure. Kiran et al in Indiain a study done in 2014 found that people of a higher socioeconomic status had a higher prevalence of VDD and limited sun exposure (16). Odhiambo et al in KNH found the prevalence of VDD in prostate cancer patients at 88.9% (25(OH)D<30ng/ml) and the mean 25(OH)D level at 19.15ng/ml. The study population had a mean age of 69 years. For 25(OH)D analysis he used the Liaison 25(OH)D assay technique and used a cut off of 25(OH)D<30ng/ml which was different from our study(17).

HAART naïve patients were 5.3 times more likely to have VDD though the numbers were too small for further analysis. This was an unexpected finding. Other studies looking at the effect of HAART on VDD have reported a higher prevalence of VDD in the patients on HAART with some few studies reporting a lower prevalence. However Gichuhi et al in AKUHhad similar findings to our study where HAART naïve patients had a higher prevalence of VDD at 49% versus 29% in patients on HAART (15).Possible explanation of this findingwould include the effect of HAART on chronic inflammation. Studies have found reduction in levels of inflammatory markers in patients started on HAART. A study by McComsey et al in 2009 reported a decrease in high sensitivity C-reactive protein, interleukin 6 and soluble vascular cell adhesion molecule-1 following treatment with HAART at 48 weeks compared to baseline(18). It is known that chronic inflammation is a risk factor for VDD. The decrease in inflammation by the HAART could possibly explain the low prevalence of VDD in the patients on HAART. In other studiesHAART was found to be a risk factor for VDD especially use

of Efavirenz (EFV). In a study by Brown et al prevalence of VDD was increased by 15% upon starting EFV based HAART and by 2% upon starting non-EFV based HAART (19). This effect by EFV results from induction of CYP24 which leads to increased catabolism of 25(OH)D(3).

A high prevalence of VDD has also been found in studies done in normal populations in Europe and North America. Studies done in normal populations in Africa are few and often involve a small sample size. A study done by Luxwolda et al (20) in 2011 among traditionally living populations in East Africa found a mean circulating 25(OH)D concentration of 46 ng/ml. The study was done among Maasai and Hadzabe communities who spend most of their time outdoors as they are pastoralist and hunters respectively (20). In contrast, preliminary data from a study done in Aga Khan University hospital by Kagotho et al found the mean 25(OH)D levels for healthy blood donors at 28.4 ng/ml (unpublished data). The prevalence of VDD (25(OH)D<20 ng/ml) was 17% (unpublished data) in this study. The study was carried out in Aga khan university hospital, a tertiary private hospital in Nairobi, Kenya. The study population consisted of 253 adult healthy blood donors of African origin. The prevalence of VDD in this study was higher than in our study which was an unexpected finding. Possible explanations include differences in socio-demographic and socio economiccharacteristics between the two populations.

Our study had two limitations; the first limitation was that the study was carried out in a single site and thus the findings may not be generalizable to the entire population. Secondly, it was a cross sectional study thus we could not assess cause effect relationship between VDD and HIV. We however were able to determine the prevalence of vitamin D deficiency in our population.

In conclusion, in our study population of HIV infected persons in Mbagathi District hospital; we found a low prevalence of vitamin D deficiency. Given the low prevalence of VDD in this population, we would not recommend routine screening and supplementation of vitamin D based on this study.

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