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Prognostic Value of Serum Estrogen, Cortisol, Calcium and Alkaline Phosphatase Activity in Pre and Postmenopausal HIV Women at Nnewi, Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Author RUN did the study design and wrote the protocol. Authors RUN and NUS did the statistical analysis and literature searches while analyses of study and proof reading were done by authors COC and EAJ. All authors read and approved the final manuscript.

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ABSTRACT

Background: Incidence of HIV infection is increasing fastest in women, and older age and some hormonal-deficient status may place them at higher risk for bone loss and fracture. The etiology of bone mineral loss in human immunodeficiency virus (HIV) infected patients is likely multifactorial,

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involving traditional risk factors such as low body weight, hypogonadism, as well as direct effects of chronic HIV infection and antiretroviral therapy.

Aims of Study: This study was designed to assess the prognostic value of Serum estrogen, cortisol, FSH, PTH, 25) OH Vit D, calcium and alkaline Phosphatase activity in pre and postmenopausal HIV infected women at NAUTH Nnewi, Nigeria.

Material and Methods: This was a cross-sectional study carried out from 2013 to 2014. A total of 80 female participants within the age bracket of 19-45(premenopausal) and 46-80 years (postmenopausal) were randomly recruited for the study. They were grouped into: (i) HIV-infected postmenopausal females (n=20). (ii) HIV- infected premenopausal females (n=20). (iii) Control postmenopausal females (n=20). (iv) Control premenopausal females (n=20). Blood samples were collected for determination of estrogen, FSH, PTH, 25OH Vitamin D and cortisol using Enzyme linked Immunosorbent Assay (ELISA) techniques. Serum levels of calcium and alkaline phosphatase activity were analyzed using spectrophotometric methods and CD4+ T-cell count using cyflow counter.

Results: The result showed that the mean serum alkaline phosphatase and cortisol levels were significantly higher while PTH and CD4+T-cell count were significantly lower in premenopausal HIV females when compared with the corresponding values in premenopausal control females (*P=.05*). The mean serum calcium, PTH, 25OH Vit D and CD4+ T- cell count were significantly lower while cortisol was significantly higher in postmenopausal HIV infected females compared to postmenopausal Control counterparts (*P=.05*). Serum estrogen and 25OH Vit D levels and CD4+ T-cell count were significantly higher while the mean serum calcium, FSH and PTH were significantly lower in premenopausal HIV when compared with postmenopausal HIV infected females (*P=.05*).

Conclusions: The present study shows alterations in both hormonal and biochemical indices of bone minerals in HIV infected women. This demonstrates significant derangement in bone health of pre and post-menopausal HIV-infected female subjects thereby increasing the risk of pathological bone fractures and can result in possible development of osteoporosis as the HIV infection progresses in these women. The clinical implication is discussed.

Keywords: HIV infection; bone health; women; menopause.

1. INTRODUCTION

Incidence of HIV infection is increasing fastest in women, and these women are living longer with efficacious anti-retroviral therapy (ART) [1]. Older age and some hormonal-deficient status may place them at higher risk for bone loss and fracture. Previous reports have shown that bone mineral density (BMD) was reduced in ART-naïve HIV-infected women [2] as well as in ART-experienced women [3], compared with age-matched HIV controls even though, the absolute difference in bone density was relatively modest, and does not appear to be higher in ART-experienced premenopausal HIV+ women [3,4]. However, the pathogenesis of low bone density in HIV+ postmenopausal women is unclear. It could be the result of co-founders such as differences in weight, ethnic distribution, hormonal or nutritional status. Alternatively, it may be the result of a pathophysiologic interaction between estrogen deficiency and elements of HIV infection and/or treatment [1]. Studies have shown that there are several ways in which estrogen could attenuate the effects of HIV-associated bone loss. Lack of estrogen increases bone resorption, as well as decreasing the deposition of new bone that normally takes place in weight-bearing bones [5]. The amount of estrogen needed to suppress this process is lower than that normally needed to stimulate the uterus and breast gland. Estrogen down-regulates many of the pro-inflammatory cytokines (Tumor necrosis factor alpha, Interleukin-1, Interleukin-6) that increase bone resorption [6,7]. These pro-inflammatory cytokines have all been found to be elevated in HIV+ individuals [8,9] and may not be completely suppressed after ART [10,11]. Estrogen appears to down-regulate bone-marrow cell expression of receptor activator of nuclear factor kappa-B ligand (RANKL) [12], and up-regulate gene expression and protein synthesis of osteoprotegerin (OPG) [13]. In pre-menopausal subjects, estrogen could attenuate the effects of pro-inflammatory cytokines and RANKL production on osteoclastogenesis, thereby mitigating the accelerated bone demineralization associated with HIV infection and treatment. However, the decline in estradiol levels that accompanies menopause would be expected to exacerbate any cytokine-mediated increase in bone

resorption. In addition to estrogen, calcium metabolism plays a significant role in bone turnover, and deficiency of calcium and vitamin D leads to impaired bone deposition; in addition, the parathyroid glands react to low calcium levels by secreting parathyroid hormone (PTH), which increases bone resorption to ensure sufficient calcium in the blood. Estradiol increases production of OPG to diminish bone resorption. Glucocorticoids stimulate RANKL expression while inhibiting OPG synthesis by osteoblasts to enhance osteoclast proliferation and differentiation, leading to bone resorption [14]. Cortisol, a steroid hormone produced by the zona fasculata of the adrenal cortex [15] is released in response to stress and low level of blood glucocorticoids. It has been reported that Cortisol decreases bone formation, favouring long term development of bone loss and fracture [16]. Longitudinal studies are necessary to determine whether the rate of bone loss or fracture is higher in HIV-infected women, especially those who are approaching or have completed the menopausal transition. Whether or not biochemical abnormalities such as vitamin D deficiency, secondary hyperparathyroidism and increased bone turnover are related to or independent of HIV and its therapy, these women still require diagnosis and correction if possible. This study was therefore designed to assess the prognostic importance of some biochemical indices such as estrogen, cortisol, calcium, FSH, PTH, Vit D and alkaline phosphatase activity in the diagnosis, treatment and monitoring of bone health in postmenopausal and premenopausal HIV infected women.

2. MATERIALS AND METHODS

2.1 Study Area

The study was carried out at the department of Institute of Human Virology (IHV) in Nnamdi Azikiwe University Teaching hospital, Nnewi (NAUTH), Anambra State, Nigeria.

2.2 Study Population

HIV infected postmenopausal and premenopausal women, within the age bracket of 46-80 and 19-45 years respectively were randomly recruited for the study. The remaining were non HIV-infected premenopausal and postmenopausal women within the same age brackets who were recruited as Control subjects amongst NAUTH hospital staff.

2.3 Study Design

This was cross-sectional study carried out from 2013 to 2014. A total of 80 (eighty) premenopausal and postmenopausal women aged (19-45) and (46-80) years respectively were randomly recruited for the study. 40 participants were HIV-1 seropositive women and were grouped as (i) HIV infected premenopausal women (n =20), (ii) HIV infected postmenopausal women (n=20). The remaining 40 participants were apparently healthy women without HIV infection which served as control and were grouped as (iii) Control premenopausal women (n= 20) and (iv) Control postmenopausal women (n = 20). HIV-seronegative control women were only volunteers amongst the hospital staff of NAUTH, Nnewi. Menopausal status was prospectively captured during interviews with structured questionnaires. Premenopausal status was evaluated by history as regular menses with greater than 6 cycles per year that were between 19-45 years. Postmenopausal status was defined by a minimum of 1 year of amenorrhea and with FSH concentration > 30 mIU/ml who were between 46-80 years. Women were screened by history and biochemical evaluation for conditions or medications known to affect bone metabolism. Medical, surgical, and reproductive history, current and past medications were obtained by interview using structured questionnaires. All control subjects met the same criteria.

2.4 Sample Processing and Storage

The blood sample was withdrawn from the antecubital vein by means of sterile plastic syringes and vacutainer EDTA bottle and plain container and, allowed to clot and centrifuged for 5 minutes at 4000 rpm for proper separation of the serum. After centrifugation, the serum samples were separated and stored frozen until analysis of calcium, FSH, PTH, 25OH Vitamin D, alkaline phosphatase, estrogen and cortisol. Whole blood was used for determination of CD4+T-cell.

2.5 Inclusion Criteria

Only participants adjudged to be HIV stage 1 were recruited for the study. Of all the subjects screened, only 80 women were eligible for the study 50% of HIV-1 seropositive women versus 50% of HIV seronegative control women were eligible. 25% of premenopausal HIV women versus 25% of premenopausal control women

were eligible and recruited. 25% of postmenopausal HIV women versus 25% of postmenopausal Control women were eligible and recruited.

2.6 Exclusion Criteria

Participants who were HIV stage 2 and stage 3 were excluded. Participants on anti-retroviral therapy were excluded from the study. Those women on contraceptives and supplements were not recruited and women who smokes or/and takes alcohol were also excluded. HIV women with untreated hyperthyroidism; renal or liver dysfunction; current pregnancy or lactation; intestinal malabsorption due to any cause; women with history of malignancy other than non-melanomatous skin cancer; metabolic bone diseases; organ transplantation; fragility fracture; and drug exposures affecting bone metabolism, endocrinopathies, current hormone replacement therapy, or past treatment of osteoporosis, women with history of hysterectomy were also excluded.

2.7 Methods

Total serum calcium was estimated as described by Sarkar & Chauhan [17].

Serum alkaline phosphatase activity was estimated using King Armstrong method as described by McComb et al. [18].

FSH and Estradiol was determined using Enzyme Immunoassay (EIA) kit as describe by Wennink et al. [19] and Tsang et al. [20] while Quantitative determination of Cortisol was also done using Enzyme Immunoassay Test kit as described by Engvall & Perlman [21].

25OH Vitamin D and PTH were determined using immune enzymatic colorimetric method Diametra, [22,23].

The body mass index (BMI) was calculated by dividing the weight (kg) by height square (m^2).

2.8 Statistical Analysis

Continuous variables and categorical data were analyzed using independent sample *t*-tests and analysis of Variance using version 17 of SPSS package. The variables were expressed as mean (±SD) and post-hoc (LSD) were used to assess significant mean differences. All *p*-values were two-tailed, and a *P*=.05 was considered statistically significant.

3. RESULTS

3.1 Anthropometric and Biochemical Characteristics in Premenopausal HIV and Premenopausal Control Female Subjects

The results showed the mean ±SD age was not significantly different between premenopausal HIV (34±1) and premenopausal control (35±1) females (*P>.05*). BMI (kg/m^2) was significantly lower in premenopausal HIV (26.66±4.70) when compared with premenopausal control (28.40±5.10) females (*P=.05*). The mean serum alkaline phosphatase (mmol/l) activity and cortisol (ng/ml) levels in premenopausal HIV females (47.23±12.02, 28.01±11.31) were significantly higher when compared with the value in premenopausal Control females (31.09±6.69, 15.21±6.47) (*P=.05* respectively). There were no significant difference in the mean serum calcium (mmol/l), estrogen (pg/ml), FSH (mIU/µl) and 25OH Vit D ng/ml levels in premenopausal HIV females (2.14±0.68, 18.50±9.09, 10.14± 4.20, 37.10±13.18) when compared with the corresponding values in premenopausal Control females (2.14±0.08, 16.76±7.99, 7.04± 3.00, 40.55±15.67) (*P>.05* respectively). However, the mean serum PTH (pg/ml) was significantly lower in premenopausal HIV females (22.40±7.40) when compared with premenopausal Control female (39.40±7.40) subjects (*P=.05*) Also, the mean CD4 T-cell count (cells/µ) in premenopausal HIV females (528.50±181.43) was significantly lower when compared with premenopausal Control (668.70±185.82) female (*P=.05*) (See Table 1).

3.2 Anthropometric and Biochemical Characteristics in Postmenopausal HIV and Postmenopausal Control Female Subjects

The mean (±SD) age in was significantly lower in postmenopausal HIV females (61±2) when compared with postmenopausal control (64.±2) (*P=.05*). Also, BMI (Kg/m^2) was significantly lower in postmenopausal HIV females (25.50±0.70) when compared with the control female counterparts (28.60±5.40) (*P=.05*). However, the mean serum Alkaline Phosphatase (mmol/L) activity, Estrogen (pg/ml), and FSH mIU/µl were not significantly different between

postmenopausal HIV (51.22±21.74, 8.42±6.58, 62.21±12.40) and postmenopausal control (49.09±14.48, 13.90±6.61, 60.05±10.20) female subjects (*P>.05* respectively). On the other hand, the mean serum calcium (mmol/L), PTH pg/ml and 25OH Vit D ng/ml levels were significantly lower in postmenopausal HIV (1.17±0.12, 35.10±2.48, 21.09±10.73) when compared with postmenopausal control (2.22±0.66, 42.89±14.57, 34.07±9.73) female subjects (*P=.05* respectively). The mean cortisol (ng/ml) level in postmenopausal HIV (27.77±16.93) was significantly higher when compared with postmenopausal control (18.29±11.20) female subjects (*P=.05*). However, CD4 T-cell count (cells/μ) was significantly lower in postmenopausal HIV (427.752±26.88) when compared with postmenopausal control (675.72±191.20) female subjects (*P=.05*) (See Table 2).

3.3 Anthropometric and Biochemical Characteristics in Premenopausal and Postmenopausal HIV Females

The mean (±SD) age was significantly lower in premenopausal HIV (32±1) when compared with postmenopausal HIV (61±2) female subjects (*P=.05*). BMI (kg/m^2) was significantly higher in premenopausal HIV (26.66±4.70) when compared with postmenopausal HIV (25.50±0.70) female subjects (*P=.05*). The mean serum alkaline phosphatase (mmol/L) and cortisol (ng/ml) levels were not significantly different between premenopausal HIV female (47.23±12.02, 28.01±11.31) and postmenopausal HIV females (51.22±21.74, 27.77±16.93) (*P>.05* respectively). However, the mean serum calcium (mmol/L), Estrogen (Pg/ml), and 25OH Vit D (ng/ml) were significantly higher in premenopausal HIV (2.14±0.68, 18.50±9.09, 37.10±13.18) when compared with postmenopausal HIV (1.17±0.12, 8.42±6.58, 21.09±10.73) female subjects (*P=.05* respectively). The mean serum FSH (mIU/μl) and PTH (pg/ml) were significantly lower in premenopausal HIV (10.14± 4.20, 22.40±7.40) when compared with postmenopausal HIV (62.21±12.40, 35.10±2.48) females (*P=.05*). Similarly, CD4+T-cell count (cells/μ) was significantly higher in premenopausal HIV (528.50±181.43) when compared with postmenopausal HIV (427.75±26.88) female subjects (*P=.05*) (See Table 3).

4. DISCUSSION

The significantly lower body mass index observed between premenopausal, postmenopausal HIV infected females and their control female counterparts suggests that HIV infected subjects were lighter than the control females. The significantly lower age difference in postmenopausal HIV compared to postmenopausal control females suggest that HIV infected females could attain menopause earlier than their control counterparts. This could place them at high risk of future bone demineralization and fractures. The present study is consistent with previous reports [24,25]. Bolland et al. [26] explained that HIV-infected patients are lighter than control subjects and suggested that low BMI could be considered a mediator in the relationship HIV–low bone mineral density. They concluded that low body weight can largely be responsible for the higher prevalence of reduced BMD found in HIV infected patients.

Table 1. Comparison of anthropometric and biochemical characteristics in premenopausal HIV and premenopausal control female subjects

Parameters	Premenopausal HIV females (n=20) (Mean±SD)	Premenopausal control females (n=20) (Mean±SD)	T- value	P-value
Age (years)	32±1	33±1	0.690	0.210
BMI (kg/m^2)	26.66±4.70	28.40±5.10	7.901	0.001
Calcium (mmol/L)	2.14±0.68	2.14±0.08	-0.856	0.398
Alkaline Phos (mmol/L)	47.23±12.02	31.09±6.69	-5.244	0.000
Estrogen (pg/ml)	18.50±9.09	16.76±7.99	-0.641	0.526
Cortisol (ng/ml)	28.01±11.31	15.21±6.47	-4.393	0.000
FSH mIU/μl	10.14± 4.20	7.04± 3.00	-0.568	0.641
PTH pg/ml	22.40±7.40	39.40±7.40	7.880	0.007
25OH Vit D ng/ml	37.10±13.18	40.55±15.67	0.676	0.404
CD4 T-cell count cells/μ	528.50±181.43	668.70±185.82	10.974	0.023

Table 2. Anthropometric and biochemical characteristics in postmenopausal HIV and postmenopausal control female subjects

Parameters	Postmenopausal HIV females (n=20) (Mean±SD)	Postmenopausal control females (n=20) (Mean±SD)	T- value	P- value
Age (years)	61±2	64±2	7.120	0.001
BMI (kg/m^2)	25.50±0.70	28.60±5.40	-4.533	0.000
Calcium (mmol/L)	1.17±0.12	2.22±0.66	-4.625	0.009
Alkaline Phos (mmol/L)	51.22±21.74	49.09±14.48	-0.364	0.718
Estrogen (pg/ml)	8.42±6.58	13.90±6.61	2.622	0.113
Cortisol (ng/ml)	27.77±16.93	18.29±11.20	-2.105	0.043
FSH mIU/µl	62.21±12.40	60.05±10.20	0.993	0.753
PTH pg/ml	35.10±2.48	42.89±14.57	4.334	0.014
25OH Vit D ng/ml	21.09±10.73	34.07±9.73	0.417	0.045
CD4 T-cell count cells/µ	427.752±26.88	675.72±191.20	4.888	0.011

Table 3. Comparison of anthropometric and biochemical characteristics in premenopausal and postmenopausal HIV females

Parameters	Premenopausal HIV female (n=20) (Mean±SD)	Postmenopausal HIV females (n=20) (Mean±SD)	T-value	P-value
Age (years)	32±1	61±2	10.441	0.000
BMI (kg/m^2)	26.66±4.70	25.50±0.70	-2.898	0.031
Calcium (mmol/L)	2.14±0.68	1.17±0.12	-4.882	0.014
Alkaline phos (mmol/L)	47.23±12.02	51.22±21.74	-0.718	0.478
Estrogen (Pg/ml)	18.50±9.09	8.42±6.58	4.011	0.000
Cortisol (ng/ml)	28.01±11.31	27.77±16.93	0.065	0.948
FSH (mIU/µl)	10.14± 4.20	62.21±12.40	4.993	0.000
PTH (pg/ml)	22.40±7.40	35.10±2.48	5.794	0.004
25OH Vit D (ng/ml)	37.10±13.18	21.09±10.73	0.497	0.043
CD4+T-cell count (cells/µ)	528.50±181.43	427.752±26.88	-4.551	0.030

The present study showed that mean serum FSH was significantly higher while estrogen level was significantly lower in HIV infected postmenopausal females when compared with the value in HIV infected premenopausal females. This finding is in accordance with a similar study reported by Guthrie and Dennerstein, [26]. The authors explained that estrogen deficiency is the most important cause of postmenopausal bone loss in women. Also a previous report by Zaidi and colleagues showed that estrogen deficiency causes both early and late forms of osteoporosis in postmenopausal females [27]. This, he associated with large increase in bone resorption caused by increased osteoclast activity. The lower levels of estrogen accelerate bone loss for a period of about five to eight years in postmenopausal females. Women normally loose annually an average 3% of their bone mass in the years after menopause. A recent study done by Sinnessael [5] showed that hormonal factors strongly determine the rate of bone resorption. Lack of estrogen increases bone resorption as well as decreasing the deposition of new bone that normally takes place in weight bearing bones. The mean serum estrogen level in HIV-infected premenopausal females showed an insignificant increase when compared with premenopausal Control group. Low bone mineral density is a recognized complication associated with HIV infection. The viral infection induces pro-inflammatory cytokines eg TNF-α and OPG which affects osteoblast and osteoclast development [28]. A study by Waugh et al. [29] showed that estrogen suppresses osteoclastogenic cytokine production in T- cells and osteoblast. It plays a role in bone metabolism focusing on pro-inflammatory cytokines and prostaglandin. These factors increase bone resorption [29]. A previous report has also shown that in pre-menopausal subjects, estrogen could attenuate the effects of pro-inflammatory cytokines and RANKL production on osteoclastogenesis, mitigating the accelerated

bone demineralization associated with HIV infection and treatment [30].

The mean serum cortisol in HIV-infected premenopausal females was significantly higher compared to the value in premenopausal Control females. Also the mean serum level of cortisol in HIV-infected postmenopausal females was statistically higher compared to their corresponding Control females. Cortisol is released in response to stress and low levels of blood glucocorticoids. The finding above is in accordance with the reports done by Berk et al. [31] which showed that cortisol decreases bone formation. The authors reported that cortisol reduces bone formation favouring long term development of osteoporosis. Cortisol suppresses many aspects of the immune system and response including the proliferation of the lymphocytes, the activities of natural killer cells, macrophages and the production of certain cytokines [32]. It has also been shown that the condition of overt hypercortisolism also leads to osteoporosis and fractures in up to 70% cases [28]. A recent study done by Bolland et al. [25] showed that high cortisol levels are seen in individuals with many types of severe acute or chronic illness and HIV/AIDS is no exception. Wester et al. [33] also showed that adrenal insufficiency occurs in Human immunodeficiency virus (HIV)/ Acquired immunodeficiency syndrome (AIDS) causing morbidity and mortality in HIV patients. Elevated cortisol levels inhibit osteoblast formation and cell proliferation. This dramatically decreases bone building and lowers bone density.

The mean serum level of calcium in HIV infected postmenopausal females was found to be significantly lowered when compared with premenopausal HIV and postmenopausal control female subjects. Report has shown that declining ovarian function before menopause is accompanied by reduction in bone mass and altered calcium metabolism [34]. Estrogen deficiency may also induce calcium loss due to decreased intestinal calcium absorption and decreased renal calcium conservation [35,36]. Calcium is an essential nutrient and it is the most abundant in the body. The finding above is similar with the reports by Heaney [37], which showed that low calcium intake may be a risk factor in the development of osteoporosis. Calcium deficiency causes mobilization of bone and leads sooner or later to osteoporosis. Loss of bone starts in women at the time of menopause and in men at about age 55 and leads to an increase in fracture rates in both sexes. Nordin [38], explained that there is a rise in obligatory calcium excretion at menopause which increases the theoretical calcium requirement in postmenopausal women to about 25 mmol (1000 mg). In the same vein, Hellman et al. [39], showed that there is impaired parathyroid hormone secretion in HIV infected patients even in the absence of parathyroid infiltrative disease thus decreasing intestinal absorption of calcium.

The present study also reported significantly higher PTH with significantly lower vitamin D levels in postmenopausal HIV infected females when compared with premenopausal HIV female counterparts. Study done by Hamid et al. [40] showed that the Levels of serum PTH increase progressively with age in women and correlate significantly with increase in bone turnover. Estrogen deficiency may also play a permissive role in the pathogenesis of age related increases in serum PTH and bone turn over [41]. It has been shown that inadequate calcium and vitamin D may lead to reduced intestinal calcium absorption, increased serum parathyroid hormone concentration and bone loss [42]. The result also showed significantly lower PTH level in both pre and postmenopausal HIV when compared with the corresponding control female subjects. Previous studies have reported significantly lower levels of PTH in HIV seropositive subjects compared to HIV seronegative control subjects [43,39,44]. The authors attributed the decrease to direct effect of the HIV on the parathyroid cells which express receptors with similarity to CD4 molecules which then acts as cellular receptors for HIV and facilitates access of the virus to immune cells [39].

The study shows significantly higher alkaline phosphatase activity in premenopausal HIV infected females when compared with the Control counterparts. Previous studies have reported that the raised alkaline phosphatase in HIV infection could be either of hepatic or of bone origin [45] and this may remain elevated for several months even after treatment suggesting increased bone turnover which continues even after restoration of a normal metabolic rate [46]. The insignificant difference observed in the mean serum alkaline phosphatase activity between HIV-infected postmenopausal females and their Control counterpart was similar to the research work carried out by Gibellini et al. [47]. The authors explained that several HIV proteins may

affect the functionality and maturation of osteoblasts, inducing apoptic stimuli in mesenchymal stem cells which are precursors of osteoblast. In particular, HIV- 1-gp120 and p55gag can reduce bone alkaline phosphatase activity and calcium deposition by osteoblast.

The study shows that CD4 T-cell count was significantly lower in both premenopausal and postmenopausal HIV when compared with the corresponding control female subjects this is consistent with previous work done on CD4 T-cell count in HIV infected women by Ukibe et al. [48]. This was attributed to reduction in cellular immunity which is the hallmark of HIV infection. However, CD4+T-cell were significantly higher in premenopausal HIV when compared with postmenopausal HIV female subjects. This was similar to the study by Kojic et al. [49]. The authors reported that menopausal status may also contribute to lower CD4 counts adding that with age and menopause, quantity of thymic tissue is reduced, and this has implications for immunologic status [49]. Van Benthem and colleagues in a study of 382 HIV-positive women not on ART, with a known period of sero-conversion, a regression analysis modeling CD4 decline found a trend for postmenopausal women having lower CD4 counts 3 years after sero-conversion compared to premenopausal women [50]. Thus the measurement of the serum levels of these parameters can be used in line with CD4 count for the assessment of some bone associated disorders in HIV infection.

5. CONCLUSION

Conclusively, the present study showed significant alterations in both hormonal and biochemical indices of bone minerals as revealed by changes in levels of estrogen cortisol, PTH, FSH, 25OH Vit D and also characteristic changes in calcium, alkaline phosphatase activity and CD4+t-cell count in HIV-infected premenopausal and postmenopausal women than in healthy women of similar age and menstrual status. Postmenopausal HIV-1 infected women have significantly lower levels of calcium, PTH, vitamin D and CD4+ T-cell count with higher serum level of cortisol when compared with the corresponding Control female subjects. There were significantly lower levels of estrogen, calcium and vitamin D and CD4+ T-cell count with higher levels of serum FSH and PTH in postmenopausal HIV compared to premenopausal HIV females. These reveal possible risk of osteoporosis and future risk of bone fractures in these women with HIV infection. The progressive alteration of these biochemical and hormonal parameters is an indication that their measurement may be useful tools for proper diagnosis; prognosis and management of bone disorders associated with menopausal HIV infected women in a low income setting. Larger longitudinal study of bone mineral density is recommended for proper insight to progress of bone demineralization and better management of menopause in HIV infected women.

6. LIMITATION OF THE STUDY

The limitation of this study includes lack of specific information with regard to the nutritional status, Dual Energy X-ray Absorptiometry (DEXA) for BMD and risk factors of osteopenia/osteoporosis in HIV infected women.

CONSENT

All authors hereby declare that written informed consent was obtained from all the patients who participated in this study.

ETHICAL APPROVAL

All authors hereby declare that all experiment and procedure have been examined and approved by the appropriate board of ethics committee of Nnamdi Azikiwe University Teaching Hospital Nnewi, South East Nigeria, and research have therefore been performed in accordance with the standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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