Original Article

The Impact of 6-month Micronutrient Supplementation on Viral, Immunological, and Mental Health Profile of a Cohort of Highly Active Antiretroviral Therapy-Naive HIV-Positive Patients in Northern Nigeria

Victor Obiajulu Olisah, Tajudeen Abiola[1], Christopher I. Okpataku[2], Reginald O. Obiako[3], Ishaq A. Audu, Bashir A. Yakasai[4]

Department of Psychiatry, Ahmadu Bello University Teaching Hospital, [3]Department of Medicine, Ahmadu Bello University, Zaria, [1]Department of Clinical Services, Medical Services Unit, Federal Neuropsychiatric Hospital, [4]Department of Internal Medicine, Kaduna State University, Kaduna, Kaduna State, [2]Department of Psychiatry, College of Health Sciences, Bingham University, Jos, Plateau State, Nigeria

Abstract

Background: HIV is a chronic disease with inflammatory reactions involving numerous elements of the immune system, resulting in an increased risk for other physical and psychiatric morbidities. Micronutrients, some of which possess anti-inflammatory properties, may help prevent the development of psychological disorders such as anxiety and depression in people living with HIV disease. **Objectives:** This study examined the profile of viral load, CD4 cell count, C-reactive protein, anxiety, and depression among highly active antiretroviral therapy (HAART)-naive HIV-positive patients receiving micronutrient supplementation over a 6-month period. **Materials and Methods:** A total of ninety HAART-naïve HIV-infected patients completed the Hospital Anxiety Depression Scale. Their blood samples were taken for serum viral load, CD4 cell count, and C-reactive protein at baseline. They all received a micronutrient supplement for 6 months, and 68 participants who remained in treatment at 6 months were reassessed with the same parameters. **Results:** After 6 months of micronutrient supplementation, the participants were found to have statistically significantly lower mean scores on the anxiety (t-test = 2.970, P = 0.003) and depression (t-test = 3.843, P = 0.001) subscales. They also had statistically significantly lower median CD4 cell count (P = 0.00) and C-reactive protein serum measures (P = 0.04). The median viral load decreased although the difference was not statistically significant. **Conclusion:** Micronutrient supplementation may reduce inflammatory reactions, anxiety, and depression in HAART-naive HIV-infected persons.

Keywords: Anxiety, CD4 count, depression, highly active antiretroviral therapy-naive, HIV, micronutrients, Nigeria, viral load

Introduction

Nigeria has the second largest HIV epidemic in the world[1] and about 3.2 million people were living with HIV in 2016.[2] Despite this large number, most of the research work have centered around disease prevalence and physical complications rather than their mental health burden. Several studies have shown that deficiencies of serum micronutrients are common among HIV-infected persons, especially those in developing countries.[3,4] Micronutrient deficiencies have been found to occur at the early stages of HIV infection, and are associated with an increased risk of HIV disease progression and mortality.[5] Micronutrient deficiencies may contribute to the pathogenesis of HIV infection through increased oxidative stress and compromised immunity.[6] Micronutrient supplements can delay HIV disease progression and reduce mortality in HIV-positive persons not receiving highly active antiretroviral therapy (HAART).[7] With the transition to more universal access to HAART, a better understanding of micronutrient deficiencies and the role of micronutrient supplements in HIV-positive persons, especially in relation to disease progression and psychological well-being, has become a priority.

Access this article online

Quick Response Code:

Website: www.nigeriamedj.com

DOI: 10.4103/nmj.NMJ_74_19

Address for correspondence: Dr. Victor Obiajulu Olisah, Department of Psychiatry, Ahmadu Bello University Teaching Hospital, Shika, Zaria, Kaduna State, Nigeria.
E-mail: olisahvictor@yahoo.com

How to cite this article: Olisah VO, Abiola T, Okpataku CI, Obiako RO, Audu IA, Yakasai BA. The impact of 6-month micronutrient supplementation on viral, immunological, and mental health profile of a cohort of highly active antiretroviral therapy-naive HIV-positive patients in Northern Nigeria. Niger Med J 2019;60:149-55.

Furthermore, studies have provided evidence that micronutrients directly intervene in immunological regulatory systems and participate in the regulation of inflammatory reactions, hence combating the incidence and progress of some physical and psychological disorders such as diabetes, atherosclerosis, anxiety, and depression, in which inflammatory processes have been found to play a role in their pathogenesis.[8,9] In addition to the immune-modulatory potential of beta-carotene and the anti-inflammatory properties of Omega-3 fatty acids and Vitamin D, the antioxidant Vitamins C and E could be important because there appears to be a connection between oxidative stress and inflammation.[9] Oxidative stress plays an important part in the onset and persistence of chronic inflammatory processes which can damage blood vessels and other tissues in the long term: A high concentration of oxygen radicals leads to the increase in the serum concentration of certain pro-inflammatory proteins such as C-reactive protein and interleukins which are indicator proteins for inflammation.[10,11] Antioxidant micronutrients can bind and neutralize oxygen radicals and thus combat the initiation of inflammation.

The levels of C-reactive protein have been found to be associated with HIV disease progression independent of CD4 lymphocyte counts and HIV RNA levels. In addition, regardless of progression to AIDS, HIV-infected individuals have a significant increase in C-reactive protein over time.[12] Studies have found that elevated levels of C-reactive protein are associated with an increased risk for psychological distress, anxiety, and depression in the general population.[13-16] A study found that anxiety as well as co-morbid anxiety and depression can be associated with an increased risk for low-grade inflammation in males at population level.[16] Hence, micronutrients with anti-inflammatory properties may reduce inflammation in patients with HIV and consequently reduce anxiety and depression that are prevalent in these patients.[17]

CD4+ T-cells are fundamental to the development of specific immune responses to infection, particularly intracellular pathogens. As the primary target of HIV, depletion of CD4+ T-cells severely limits the host response capacity.[18] The CD4+ T-cell count is the most significant predictor of disease progression and survival.[19,20] Lower CD4 counts are associated with greater risk of disease progression over time. The value of HIV viral load measurement as a prognostic marker has long been established.[21] An approximately inverse relationship to the CD4 cell count and survival time has been observed in around 80% of patients.[22] Higher viral load levels are associated with more rapid decline of CD4 cells, assisting prediction of the rate of CD4 count decline and disease progression.

More recent evidence on brain metabolism suggests that nutritional deficiencies of certain micronutrients can influence the development and progression of mental illnesses.[23-25] Some studies have shown that the intake of antioxidant micronutrients (zinc, selenium, and Vitamin C) correlated negatively with the development of anxiety, depression, and stress in HIV-positive individuals.[6] Folic acid and Vitamin B6 help combat depression.[24-26] Zinc and Vitamin B12 deficiency has been associated with the development of several psychiatric disorders such as depression, bipolar disorder, panic disorder, schizophrenia, and phobias.[27,28]

Therefore, micronutrient supplementation should be seen as an important aspect of HIV treatment and support in a resource-poor country like Nigeria where significant gaps persist in providing antiretroviral treatment to all who are in need. Less than 60% of the people living with HIV in sub-Saharan Africa have access to antiretroviral therapy (ART).[2] Most times, patients had to wait until their CD4 counts drop below 200 before the commencement of ART and to this end, micronutrient supplementation could serve as a pragmatic stop gap.

However, most studies on micronutrient supplementation in HIV/AIDS have focused on its effect on the physical outcomes of the disease rather than psychological. People living with HIV are about two to three times more likely to experience mental health disorders during the course of their illness, especially anxiety and depression, than the general population which, in turn, reduce their quality of life and adherence to antiretroviral treatment and contribute significantly to disease progression and premature deaths.[17] For these reasons, it is important that physicians in the care of patients with HIV/AIDS should not neglect their mental health.

In this study, we looked at what happens to the viral load, CD4 cell count, C-reactive protein (biomarker for inflammation), anxiety, and depression among HAART-naive HIV-positive patients receiving micronutrient supplementation over a 6-month period in Northern Nigeria.

Materials and Methods

This study was part of a larger study on the effects of micronutrients on immunological outcomes of HAART-naive patients with HIV infection in Kaduna State conducted by some physicians at a tertiary health institution in Nigeria.

Sample size and technique

A minimum sample size of 88 was determined from the Fisher's sample size formula for longitudinal studies, as follows:[29] $N = Z^2 P (1 - P)/d^2 \times 1 (1 - f)$, where N = desired sample size when population is over 100,000; Z = confidence interval at 95% (1.96); P = prevalence rate of HIV infection in Kaduna State, Nigeria (5.1%);[30] d = sampling error at 5% (0.05); and f = attrition rate of 10%. However, in order to increase the power of the study, ninety HIV-positive HAART-naïve adult patients, aged 18–59 years, were recruited at baseline through consecutive sampling of every eligible patient meeting the inclusion criteria at the clinics during the study period. The research lasted for 3 years, from September 2013 to September 2016.

Study design

A longitudinal study.

Study population

The study participants were ninety HAART-naïve and newly diagnosed HIV-infected patients who were not eligible for ART medication on the basis of their CD4 count of 500 and above. They were recruited from HIV clinics of two major hospitals in Kaduna State, Nigeria, namely the Nasara HIV Treatment and Care Centre at Ahmadu Bello University Teaching Hospital, Zaria, and the Caritas Catholic Relief Foundation (CCRF) HIV Centre at Saint Gerard's Catholic Hospital, Kaduna State, Nigeria. Both the centers provide free ART to eligible patients and supportive care to ART-ineligible patients. All the patients presenting to the study centers during the period of the study who met the inclusion criteria were recruited until the sample size of ninety participants was attained.

Inclusion criteria for the ninety HIV-infected patients

Participants were aged 18–59 years, were physically fit, and were mentally alert, without evidence of physical deformity. Other eligibility criteria were HAART naïve, being in the WHO clinical Stages I and II, and CD4+ count >500 cells/μl.

Exclusion criteria

Participants were excluded from the research if they had a history of alcohol and substance abuse, past psychiatric history, chronic hepatitis B or C or HIV-2 infection, vegetarian diet, chronic hypertension, and immunosuppressive illnesses (such as diabetes mellitus, chronic renal disease, malignancy, and sickle cell anemia). Other exclusion criteria were refusal to give consent to participate, pregnancy, presence of AIDS-defining illness, and default from one clinic visit.

Enrollment and evaluations of HIV-infected antiretroviral therapy-naïve patients

At the various enrollment centers, all the patients meeting the inclusion criteria were educated and counseled on the various aspects of HIV care and support by nurse HIV counselors, before the research objectives and protocol were explained to them, with emphasis on the voluntary nature of the study and assurance of the confidentiality of their data. After signing an informed written consent, the sociodemographic data and a history of illness were obtained from all patients, and they completed the Hospital Anxiety Depression Scale (HADS). 20 ml of whole venous blood samples was collected from each patient for plasma HIV RNA load; CD4+ T-cell counts; serum zinc, copper, and Vitamin B12 levels; and C-reactive protein at baseline. All the participants received daily doses of one capsule of a micronutrient supplement for 6 months and were reassessed with the same instruments and laboratory parameters at 6 months. Blood samples were also collected from ninety healthy HIV-negative volunteers and were assayed for serum levels of Vitamin B12, zinc, and copper.

Instruments of study

Sociodemographic questionnaire

A sociodemographic questionnaire containing sociodemographic data and illness-related information was designed by the authors.

Hospital Anxiety Depression Scale

The HADS is a portable, easy-to-administer measure that screens for the presence of anxiety or depressive state of both clinical and nonclinical population. It consists of seven depression items and seven anxiety items and has been validated for use in Nigeria.[31] A score of 8 and above on either of the two components is regarded as case.

Micronutrient supplements

The micronutrient supplement used in the study was a capsule containing a mixture of 11 vitamins (A, B1, B2, B3, B6, B12, biotin, folate, pantothenate, C, and E), 6 trace elements (selenium, copper, zinc, ferrous, molybdenum, and manganese), 2 electrolytes (potassium and magnesium), 2 essential amino acids (L-glycine and L-lysine), and 1 peptide (choline bitartarate).

Ethical certification of research proposal

The research proposal was reviewed and approved by the Institutional Health Research Ethical Committee of the two hospitals.

Data analysis

The IBM-SPSS version 21 (IBM SPSS Inc. 2012, Armonk, New York) statistical package was used for data entry and analysis. Data were analyzed by descriptive statistics including frequencies, percentages, means, and standard deviation. The Chi-square test was used to characterize the significance of the difference between categorical variables, whereas *t*-test statistics was used to characterize the significance of the difference between mean scores. All statistical evaluations were considered significant at $P < 0.05$, two tailed.

Results

A total of ninety participants were recruited for the study at baseline, but only 68 (75.6%) of them completed the study at 6 months. Twenty-two participants were unable to complete the study at 6 months for various reasons including loss to follow-up, default from a clinic visit, drop in CD4 count below 500 cells/μl, and pregnancy.

Majority of the participants at baseline were <41 years in age (62.2%), belong to female gender (76.7%), were of the Christian faith (81.1%), had at least 12 years of formal education (88.9%), currently unmarried (53.3%) as at the time of assessment, and gainfully employed (75.6%). There was no significant difference between the sociodemographic characteristics of participants at baseline and at 6 months as shown in Table 1.

The median serum levels of Vitamin B12, copper, and zinc of the HIV-positive, HAART-naive participants at baseline were significantly lower than those of the HIV-negative control group. After 6 months of supplementation, the levels of micronutrients among the HIV-positive, HAART-naive participants increased statistically significantly (Vitamin B12: $P = 0.02$, copper: $P = 0.00$, and zinc: $P = 0.00$), as shown in Table 2.

The point prevalence of anxiety and depression among participants at baseline was 23.2% and 23.2%, respectively. After 6 months of micronutrient supplementation, the point prevalence of anxiety and depression was 13.2% and 4.4%, respectively, as shown in Table 3.

A cross tabulation of the mean scores for anxiety and depression at baseline and after 6 months of micronutrient supplementation among the participants showed a statistically significantly lower HADS mean scores for anxiety ($P = 0.003$) and depression ($P = 0.001$), as shown in Table 4.

Table 1: Sociodemographic characteristics of HIV-infected, highly active antiretroviral therapy-naïve patients at baseline and at 6 months of treatment with micronutrient supplementation

Characteristics	At baseline ($n=90$; 100.0), *n* (%)	At 24 weeks ($n=68$; 75.6), *n* (%)	χ^2, *P*
Age group (years)			
≤20	2 (2.2)	2 (2.2)	2.284, 0.3
21-40	54 (60.0)	38 (42.2)	
41-60	34 (37.8)	28 (31.2)	
Gender			
Female	69 (76.7)	51 (56.7)	0.432, 0.5
Male	21 (23.3)	17 (18.9)	
Religion			
Christianity	73 (81.1)	57 (63.3)	1.336, 0.3
Islam	17 (18.9)	11 (12.2)	
Marital status			
Married	42 (46.7)	30 (33.3)	1.101, 0.8
Never married	26 (28.9)	20 (22.2)	
Widowed	14 (15.6)	11 (12.2)	
Divorced/separated	8 (8.9)	7 (7.8)	
Education			
Secondary	46 (51.1)	35 (38.9)	1.391, 0.5
Tertiary	34 (37.8)	24 (26.7)	
Primary	10 (11.1)	9 (10.0)	
Occupation			
Self-employed	32 (35.6)	28 (31.1)	9.315, 0.1
Government worker	21 (23.3)	16 (17.8)	
Private business worker	15 (16.7)	8 (8.9)	
Not employed	22 (24.4)	16 (17.7)	

The initial HIV RNA load, CD4 cell count, and C-reactive protein median values were compared with the values obtained after 6 months of micronutrient supplementation and a drop was found in the viral load although the difference was not statistically significant ($P = 0.32$). There was a significant drop in the CD4 count ($P = 0.00$) and C-reactive protein levels ($P = 0.04$), as shown in Table 5.

Discussion

This study examined the impact of 6-month micronutrient supplementation on viral, immunological, and mental health profile of a cohort of HAART-naive HIV-positive patients in Northern Nigeria and found a decrease in the experience of anxiety and depression and a reduction in C-reactive protein (a pro-inflammatory biomarker).

The sociodemographic characteristics of the participants at baseline did not differ significantly from the values at 6 months. Most participants were aged between 21 and 40 years, with a preponderance of female gender, similar to the findings from other related studies among adult HIV-positive population in Africa.[32]

The median serum levels of micronutrients such as Vitamin B12, zinc, and copper of the HIV-positive, HAART-naive participants at baseline were significantly lower than those of the healthy HIV-negative control group. Similarly, the levels of micronutrients among the HIV-positive, HAART-naive participants increased significantly after 6 months of supplementation. This finding implied that the micronutrient supplementation was effective in improving the levels of these micronutrients in the HIV-positive participants.

The point prevalence of anxiety and depression among participants at baseline was 23.2% and 23.2%, respectively. After 6 months of micronutrient supplementation, the prevalence of anxiety and depression was 13.2% and 4.4%, respectively. The differences in both psychological parameters between baseline values and after 6 months of micronutrient supplementation were statistically significant. This finding is similar to those from other studies.[6,33] Previous studies have shown that micronutrients, especially folic acid, Vitamins B6 and B12, zinc, and some amino acids, play a role in anxiety and depression. Low levels of folic acid and Vitamin B12 have been found in studies of depressive patients, and a targeted

Table 2: Serum levels of zinc, copper, and Vitamin B12 of HIV-infected, highly active antiretroviral therapy-naïve patients at baseline compared with the levels after 6 months of micronutrient supplementation and the levels of HIV-negative healthy volunteers

Nutritional variable	HIV-infected patients at baseline ($n=90$; 100), median (IQR)	*P* value for HIV-infected patients at baseline versus healthy volunteers	HIV-infected patients at 6 months ($n=68$; 75.6), median (IQR)	*P* value for HIV-infected patients at baseline versus those at 6 months
Zinc (ppm)	0.01 (0.01-0.03)	0.00 (0.00)	0.23 (0.21-0.27)	0.00 (0.00)
Copper (ppm)	−0.4 (−0.5-0.03)	0.00 (0.00)	0.03 (0.02-0.03)	0.00 (0.00)
Vitamin B12 (ng/L)	15.0 (9.9-39.4)	0.00 (0.00)	30.0 (17.8-50.7)	0.02 (0.00)

P values for median at baseline versus 6 months were calculated using independent samples median test; independent samples Moses test of extreme reaction was used to calculate *P* values for ranges at baseline versus 6 months. $P<0.05$ is statistically significant. IQR - Interquartile range

intake of these micronutrients may have prophylactic or therapeutic effects on some mental disorders including anxiety and depression, as suggested in this study.[33,34]

The significantly lower prevalence of anxiety and depression after 6 months of micronutrient supplementation can also be viewed from the area of inflammation. Inflammatory processes have been found to play a role in the pathogenesis of anxiety and depression.[8,9] Increased levels of C-reactive protein (a marker of inflammation) have been found to be associated with HIV disease progression,[12] which correlates with the increase in the prevalence of anxiety and depression as the disease progresses.[13-16] This study found a significant reduction in C-reactive protein levels after 6 months of micronutrient supplementation. The anti-inflammatory and antioxidant properties of micronutrients may reduce inflammation that occurs naturally with HIV disease and consequently reduce C-reactive protein levels. The reduction in the inflammatory processes also has the potential to reduce the prevalence of anxiety and depression.[17]

Table 3: Prevalence of anxiety and depression at baseline and after 6 months of micronutrient supplementation among HIV-infected, highly active antiretroviral therapy-naïve patients

Variables	Noncase (%)	Cases (%)	Total (%)
HADS depression subscale			
Baseline	69 (76.7)	21 (23.3)	90 (100)
6 months	65 (95.6)	3 (4.4)	68 (100)
HADS anxiety subscale			
Baseline	69 (76.7)	21 (23.3)	90 (100)
6 months	59 (86.8)	9 (13.2)	68 (100)

HADS - Hospital Anxiety Depression Scale

Table 4: Cross tabulation of mean scores for anxiety and depression at baseline and after 6 months of micronutrient supplementation among HIV-infected, highly active antiretroviral therapy-naïve patients

Variables	Baseline (preintervention)	After 6 months (postintervention)	*t*-test	*P*
HADS				
Depression	4.66 (4.91)	2.12 (2.71)	3.843	<0.001
Anxiety	5.40 (5.13)	3.12 (4.28)	2.970	0.003

HADS - Hospital Anxiety Depression Scale

This study showed that CD4 cell count dropped significantly over a 6-month period in spite of the micronutrient supplementation. Previous studies have shown that the CD4+ T-cell count is the most significant predictor of disease progression and survival.[19,20] The implication here is that micronutrients though useful in many immunological processes in patients with HIV/AIDS, may not be very effective in treatment when used alone in slowing the fall in CD4 count during the course of HIV infection. This supports the current recommendation that people living with HIV start antiretroviral treatment as soon as possible, which is being implemented in an increasing number of countries.[35] In some countries like Nigeria, the decision about when to start treatment is still largely dependent on a CD4 count even though the updated HIV treatment guidelines in Nigeria recommend starting antiretroviral treatment regardless of CD4 count levels.[36] The best approach to treatment should be to commence micronutrient supplementation once diagnosis is made and in the dire situation where HAART is not available and when available, should at least be used as an adjunct in persons taking HAART, as both therapies have been found to be synergistic.[35] This is more so, in view of the observation in this study that micronutrient supplementation improved other important outcome measures such as mental health. An improved mental health may translate into better lifestyle, higher quality of life, and improved drug adherence, with attendant multiplier effect on slower HIV disease progression. In addition, this study showed that the median viral load of participants decreased after 6 months of micronutrient supplementation, although the difference was not statistically significant. This finding is important when taking into account the fact that viral load increases over time in the natural history of HIV infection. The reduction in viral load observed in this study over a 6-month period of micronutrient supplementation may be related to the fact that micronutrients have antiviral activity either directly or indirectly through immune modulation.[37,38]

Conclusion

This study provides preliminary evidence that micronutrients positively influence the psychological well-being and reduce the experience of anxiety and depression that is common in recently diagnosed patients with HIV. The anti-inflammatory property of micronutrients was observed through the significant reduction in C-reactive protein levels. Micronutrient supplementation did not seem to significantly slow the decline

Table 5: Initial HIV RNA load, CD4+ T-cell count, and C-reactive protein of HIV-infected, highly active antiretroviral therapy-naïve patients compared with those values after 6 months of micronutrient supplementation

Immunological variables of patients	HIV-infected patients at baseline (*n*=90; 100), median (IQR)	HIV-infected patients at 6 months (*n*=68; 75.6); median (IQR)	*P* Baseline versus 6 months
HIV RNA (copies/mL)	27,105.0 (6346.0-955,514.0)	16,227.5 (6,266.0-73,146.0)	0.32 (0.35)
CD4+ count (cells/μL)	704.5 (600.0-880.0)	561.0 (500.0-700.0)	0.00 (0.00)
CRP (ng/mL)	29.4 (12.3-68.8)	26.2 (8.8-46.8)	0.04 (0.9)

P values for median at baseline versus 6 months were calculated using independent samples median test; independent samples Moses test of extreme reaction was used to calculate *P* values for ranges at baseline versus 6 months. *P*<0.05 is statistically significant. IQR - Interquartile range; CRP - C-reactive protein

in CD4 T-cell count during the period of treatment, and this supports the current recommendation to commence HAART as early as possible. The data obtained from this study are compelling enough to warrant further studies with more appropriate design investigating the role that micronutrients might play in reducing mental illness in people living with HIV/AIDS in the community.

Even with the availability of HAART in many African societies and the current recommendation to commence treatment as early as possible in the course of the disease, complementary micronutrient supplementation should be viewed as an important and integral part of HIV and AIDS treatment to improve the general, physical, and mental health status of people living with HIV.

The study is limited by the relatively small sample size and hospital-based study design, so findings cannot be generalized to the entire population of people living with HIV. The instruments were not administered to a control group who did not receive micronutrient supplementation, and diagnostic instruments for anxiety and depressive disorders were not used.

Acknowledgment

We are grateful to the doctors and nurses at the Ahmadu Bello University Teaching Hospital, Zaria, HIV/AIDS Treatment and Care Centre, and the Saint Gerald's Catholic Hospital HIV treatment unit (CCRF HIV Centre) for their help during data collection.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. National Agency for the Control of AIDS. 'Nigeria GARPR 2015 Report. National Agency for the Control of AIDS; 2015Available from: https://naca.gov.ng/nigeria_garpr_2015_report. [Last accessed on 2016 Nov 14].
2. UNAIDS 'AIDS info'; 2016. Available from: https://www.unaids.org/en/regionscountries/countries/Nigeria. [Last accessed on 2017 Sep 14].
3. Olaniyi JA, Arinola OG. Essential trace elements and antioxidant status in relation to severity of HIV in Nigerian patients. Med Princ Pract 2007;16:420-5.
4. Bilbis LS, Idowu DB, Saidu Y, Lawal M, Njoku CH. Serum levels of antioxidant vitamins and mineral elements of human immunodeficiency virus positive subjects in Sokoto, Nigeria. Ann Afr Med 2010;9:235-9.
5. Kupka R, Msamanga GI, Spiegelman D, Morris S, Mugusi F, Hunter DJ, *et al.* Selenium status is associated with accelerated HIV disease progression among HIV-1-infected pregnant women in Tanzania. J Nutr 2004;134:2556-60.
6. Jamali F, Izadi A, Khalili H, Garmaroudi G. Correlation between daily dietary micronutrients intake and mental health outcomes in Iranians living with HIV infection. J Assoc Nurses AIDS Care 2016;27:817-25.
7. Fawzi W, Msamanga G, Spiegelman D, Hunter DJ. Studies of vitamins and minerals and HIV transmission and disease progression. J Nutr 2005;135:938-44.
8. Montero-Vega MT. The inflammatory process underlying atherosclerosis. Crit Rev Immunol 2012;32:373-462.
9. Hui DY. Phospholipase A (2) enzymes in metabolic and cardiovascular diseases. Curr Opin Lipidol 2012;23:235-40.
10. Pepys MB, Hirschfield GM. C-reactive protein: A critical update. J Clin Invest 2003;111:1805-12.
11. Nordestgaard BG. Does elevated C-reactive protein cause human atherothrombosis? Novel insights from genetics, intervention trials, and elsewhere. Curr Opin Lipidol 2009;20:393-401.
12. Lau B, Sharrett AR, Kingsley LA, Post W, Palella FJ, Visscher B, *et al.* C-reactive protein is a marker for human immunodeficiency virus disease progression. Arch Intern Med 2006;166:64-70.
13. Wium-Andersen MK, Ørsted DD, Nielsen SF, Nordestgaard BG. Elevated C-reactive protein levels, psychological distress, and depression in 73, 131 individuals. JAMA Psychiatry 2013;70:176-84.
14. Gimeno D, Kivimäki M, Brunner EJ, Elovainio M, De Vogli R, Steptoe A, *et al.* Associations of C-reactive protein and interleukin-6 with cognitive symptoms of depression: 12-year follow-up of the Whitehall II study. Psychol Med 2009;39:413-23.
15. Puustinen PJ, Koponen H, Kautiainen H, Mäntyselkä P, Vanhala M. Psychological distress and C-reactive protein: Do health behaviours and pathophysiological factors modify the association? Eur Arch Psychiatry Clin Neurosci 2011;261:277-84.
16. Liukkonen T, Räsänen P, Jokelainen J, Leinonen M, Järvelin MR, Meyer-Rochow VB, *et al.* The association between anxiety and C-reactive protein (CRP) levels: Results from the Northern Finland 1966 birth cohort study. Eur Psychiatry 2011;26:363-9.
17. WHO HIV/AIDS and Mental Health Report by the Secretariat; 20, November 2008. Available from: http://apps.who.int/gb/archive/pdf_files/EB124/B124_6-en.pdf. [Last accessed on 2017 Sep 14].
18. Chinen J, Shearer WT. Molecular virology and immunology of HIV infection. J Allergy Clin Immunol 2002;110:189-98.
19. Phillips AN, Lundgren JD. The CD4 lymphocyte count and risk of clinical progression. Curr Opin HIV AIDS 2006;1:43-9.
20. Phillips A, Pezzotti P; CASCADE Collaboration. Short-term risk of AIDS according to current CD4 cell count and viral load in antiretroviral drug-naive individuals and those treated in the monotherapy era. AIDS 2004;18:51-8.
21. Lyles RH, Muñoz A, Yamashita TE, Bazmi H, Detels R, Rinaldo CR, *et al.* Natural history of human immunodeficiency virus type 1 viremia after seroconversion and proximal to AIDS in a large cohort of homosexual men. Multicenter AIDS cohort study. J Infect Dis 2000;181:872-80.
22. Thiébaut R, Pellegrin I, Chêne G, Viallard JF, Fleury H, Moreau JF, *et al.* Immunological markers after long-term treatment interruption in chronically HIV-1 infected patients with CD4 cell count above 400×10(6) cells/l. AIDS 2005;19:53-61.
23. Hinze-Selch D, Weber MM, Zimmermann U, Pollmächer T. Thiamine treatment in psychiatry and neurology. Fortschr Neurol Psychiatr 2000;68:113-20.
24. Akhondzadeh S, Gerbarg PL, Brown RP. Nutrients for prevention and treatment of mental health disorders. Psychiatr Clin North Am 2013;36:25-36.
25. Crellin R, Bottiglieri T, Reynolds EH. Folates and psychiatric disorders. Clinical potential. Drugs 1993;45:623-36.
26. Williams AL, Cotter A, Sabina A, Girard C, Goodman J, Katz DL. The role for Vitamin B-6 as treatment for depression: A systematic review. Fam Pract 2005;22:532-7.
27. Reynolds E. Vitamin B12, folic acid, and the nervous system. Lancet Neurol 2006;5:949-60.
28. Lai J, Moxey A, Nowak G, Vashum K, Bailey K, McEvoy M. The efficacy of zinc supplementation in depression: Systematic review of randomised controlled trials. J Affect Disord 2012;136:e31-e39.
29. Araoye MO. Research Methodology with Statistics for Health and Social Sciences. Ilorin: Nathadex Publishers; 2004. p. 117-20.
30. Federal Ministry of Health. Abuja; 2010. Available from: http://www.nigeriaaids.org/documents/2010_National%20HIV%20Sero%20Prevalence%20Sentinel%20Survey.pdf. [Last accessed on 2013 Feb 08].
31. Abiodun OA. A validity study of the hospital anxiety and depression scale in general hospital units and a community sample in Nigeria. Br J Psychiatry 1994;165:669-72.
32. Olisah VO, Baiyewu O, Sheikh TL. Adherence to highly active antiretroviral therapy in depressed patients with HIV/AIDS

attending a Nigerian university teaching hospital clinic. Afr J Psychiatry (Johannesburg) 2010;13:275-9.
33. Adhikari PM, Chowta MN, Ramapuram JT, Rao SB, Udupa K, Acharya SD. Effect of Vitamin B12 and folic acid supplementation on neuropsychiatric symptoms and immune response in HIV-positive patients. J Neurosci Rural Pract 2016;7:362-7.
34. Morris MS, Fava M, Jacques PF, Selhub J, Rosenberg IH. Depression and folate status in the US population. Psychother Psychosom 2003;72:80-7.
35. World Health Organization. Guideline on When to Start Antiretroviral Therapy and on Pre-Exposure Prophylaxis for HIV. World Health Organization; September, 2015. Available from: https://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en/. [Last accessed on 2019 Jul 14].
36. Guideline on HIV Treatment in Nigeria 2016 Report. Available from: https://aidsfree.usaid.gov/sites/default/files/2016_nigeria_natl_guidelines_hiv_treat_prev.pdf. [Last accessed on 2019 Jun 25].
37. Sprietsma JE. Cysteine, glutathione (GSH) and zinc and copper ions together are effective, natural, intracellular inhibitors of (AIDS) viruses. Med Hypotheses 1999;52:529-38.
38. Cunningham-Rundles S, McNeeley DF, Moon A. Mechanisms of nutrient modulation of the immune response. J Allergy Clin Immunol 2005;115:1119-28.