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Effects of Micronutrient Supplementation on Lipid Peroxidation and Enzymatic Antioxidant System in Blood of Human Immunodeficiency Virus (HIV)-infected Adults in Sokoto, Nigeria

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Authors' contributions

This work was carried out in collaboration between all the authors. Authors LSB and YS designed the study. Author MHY did the literature searches. Authors SCD, CHN and ASM designed the protocol. The collection of samples and analysis were handled by all the authors jointly. The first draft of the manuscript was written by author MHY. All authors read, reviewed and approved the final manuscript.

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ABSTRACT

Aims: To examine the effects of micronutrient supplementation on lipid peroxidation and enzymatic antioxidant system in 210 HIV-positive adult patients.
Study Design: A randomized clinical trial was conducted comparing four groups receiving daily either a micronutrients supplement or no supplement for 12 months and the effects of micronutrients supplementation on lipid peroxidation and enzymatic antioxidant system from baseline to 12 months were assessed.
Place and Duration of Study: Antiretroviral Therapy Clinic, Usmanu Danfodiyo University Teaching Hospital, Sokoto and Department of Chemical Pathology and Immunology, Usmanu

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Danfodiyo University, Sokoto, between April, 2013 and September, 2014.
Methodology: We included 210 patients (94 men, 116 women; age range 18-50 years 106 (HAART-naïve, HIV-infected and 104 HIV-infected on HAART). Clinical examinations as well as laboratory analysis of serum activities of antioxidant enzymes superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX) and malondialdehyde (MDA) concentrations (lipid peroxidation index) were measured at baseline and measurement repeated at three-monthly period for a total of 12 months.
Results: The results showed that at baseline and 3 months follow-up, serum activities of SOD, CAT and GPX and MDA concentrations were similar ($p<0.05$) between the HAART-naïve and HIV-infected on HAART that received micronutrient supplements or no supplements. However after 6 to 12 months, serum activities of SOD, CAT and GPX significantly increased ($p<0.001$), while MDA significantly decreased ($p<0.001$) in HAART-naïve and HIV-infected on HAART that received micronutrient supplements respectively compared to unsupplemented groups.
Conclusion: The results in the current study demonstrate that, the lower serum activities of antioxidant enzymes and higher lipid peroxidation in HAART-naïve HIV-infected and HIV-infected on HAART at baseline were reversed by micronutrients supplementation in the subjects.
Recommendation: The micronutrient supplement used was tolerated and when given at nutritional doses is likely to reduce oxidative stress and may slow the HIV-disease progression and prolong the time before initiation of ART or used as an adjuvant therapy with HAART. This could reduce the morbidity and mortality in the affected HIV/AIDS patients.

Keywords: Antioxidants; enzymes; lipid peroxidation; micronutrient supplementation; HIV; Nigeria.

1. INTRODUCTION

Human immunodeficiency virus (HIV) Infection is associated with a decline in immunity and progresses to acquired immunodeficiency syndrome (AIDS). Thus a vicious cycle has been envisaged in which undernourished HIV-infected persons have micronutrient deficiencies leading to further immune-suppression and oxidative stress and subsequent acceleration of HIV replication and CD_4^+ T-cell depletion [1-2]. Micronutrient deficiencies and HIV disease progression are thought to interact synergistically progressively aggravating each other [1].

Several studies have shown that people living with HIV/AIDS are under chronic oxidative stress characterized by perturbations of the antioxidant defence system including changes in glutathione, glutathione reductase, thioredoxin, ascorbate, tocopherol, selenium and superoxide dismutase [3-7]. Elevated serum levels of hydroperoxides and malondialdehyde have been observed in HIV-positive patients and are indicative of chronic oxidative stress and may contribute to several aspects of HIV disease progression including viral replication, inflammatory response, decreased immune cell proliferation, loss of immune function and increased sensitivity to drug toxicities [4,8].

The enhanced oxidative stress during HIV infection may also be involved in the pathogenesis of impaired T-cell responsiveness and enhanced T-cell apoptosis and it may also play a role in the development of certain HIV-related clinical disorders, including malignancies and HIV- related encephalopathy [6, 9-10].

The deleterious effects of free radical induced tissue damage are to a large extent prevented by the integrated antioxidant enzyme systems that directly metabolize reactive oxygen species. These include superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase (CAT) [11-14]. The enzymatic antioxidants catalyze the transfer of electrons from a substrate towards a free radical. The reaction is coupled with NADPH that is derived from different metabolic pathways and the substrates utilized in the reactions are regenerated to be used again [15].

In order to exert their optimum catalytic activities, antioxidant enzymes need trace elements especially zinc, copper, manganese, iron and selenium as co-factors needed for the synthesis and effective antioxidant defence of the de novo antioxidant enzymes. Thus zinc is an essential co-factor for cytoplasmic superoxide dismutase (Cu-Zn SOD) enzyme [16]. Superoxide dismutase catalyses the univalent reduction and oxidation of $O_2^{\cdot-}$ to H_2O_2 and molecular O_2.

Iron (Fe) is required for catalase (CAT), a haem-protein enzyme containing four (4) haem

prosthetic groups. Catalase is concentrated mainly in the peroxisomes and mitochondria [17] where it catalyses the conversion of hydrogen peroxide (product of superoxide dismutation) into water and oxygen [18].

While selenium is an integral part of GPX an enzyme located in the mitochondrial matrix and cytosol of animal cells [18]. GPX protect cells against oxidative damage by converting the reduced glutathione (GSH) into oxidized glutathione (GSSG) removing hydrogen peroxide (H_2O_2) to form water (H_2O) [19].

Several prospective, randomized studies suggest that, micronutrients help to strengthen the immune system, improve clinical outcomes and significantly increase $CD4^+$ cell count and reduce the severity and impact of opportunistic infections in people living with HIV/AIDS [20-24].

Micronutrients play an essential role in supporting the body's immune functions and HIV-infected patients are required to have an adequate micronutrient status [11]. Timely nutritional support for people living with HIV (PLHIV) may help extend the asymptomatic period of relative health for people living with HIV or where severe immune deterioration has already occurred, it may reduce the risk of death [12]. Micronutrient supplements have been used as part of a standard care package offered in the medical management of HIV/AIDS patients. However, the results were either not well defined or conflicting as some but not all studies show immunological and clinical benefits. Antioxidant micronutrients supplementation could be a relatively low cost strategy to defer the initiation of expensive, potentially toxic and lifelong antiretroviral therapy. The current study is aimed at assessing whether a daily dosage of micronutrients supplement (Centrum®) could improve the enzymatic antioxidant system and reduce lipid peroxidation among HIV patients in Sokoto, Nigeria. The choice of Centrum® supplements were due to improvement in the antioxidant minerals and multivitamins content over those demonstrated previously by Fawzi et al. [22] and Baum et al. [25].

2. METHODS

2.1 Study Participants and Site

The study was conducted at the Antiretroviral Therapy Clinic (ART), Usmanu Danfodiyo University Teaching Hospital, Sokoto Nigeria. ART Clinic provides out-patient care and treatment for HIV-infected persons. A total of two hundred and ten (210) subjects were enrolled into the study. These consisted of 106 HAART-naïve HIV-infected which comprised of and 104 HIV-infected on HAART.

2.2 Eligibility

Enrolment of participants took place between April, 2013 and September, 2014. Eligibility criteria for the patients include; a) at least eighteen (18) years old, b) asymptomatic HIV-positive adults who are HAART-naive and HIV-infected on HAART, c) screening $CD4^+$ T lymphocytes ≥ 350 cells/µl, and d) provided written informed consent. Study subjects were ineligible if they have any of the following: a) allergy or intolerance to any study ingredient, b) be pregnant, c) have alanine transaminase (ALT) greater than three times normal range, d) have known liver cirrhosis, or serum creatinine >133 µmol/l, e) smoke cigarette, abuse alcohol or be taking micronutrient or natural health product.

2.3 Study Design

A randomized clinical trial was conducted comparing four groups receiving daily either a micronutrients supplement or no supplement for 12 months and the effects of micronutrients supplementation on lipid peroxidation and enzymatic antioxidant system from baseline to 12 months were assessed according to the method described by Hammer et al. [26]. All the HIV-positive patients were evaluated clinically by the consultant Physicians and the patients allotted to different Clinical stages of HIV-infection according to the revised criteria from the Centres for Disease Control and Prevention [27].

Eligible subjects were assigned to the following groups as shown in the study flow chart (Fig. 1).

Opportunistic illness prophylaxis and treatment and ART were offered to the patients at the Clinic according to standard treatment guidelines for the use of antiretroviral (ARV) drugs in Nigeria [28].

2.4 Screening, Baseline, and Follow-up Assessments

The HIV-infected subjects were consecutively selected from the population of HIV patients attending Antiretroviral Therapy Clinic (ART Clinic), Usmanu Danfodiyo University Teaching

Hospital Sokoto. Potential participants were identified by preliminary screening at routine Clinic visits and consecutively selected until the desired sample size was attained. Following informed consent, a structured interviewer-administered questionnaire was used to elicit data on subject's socioeconomic and demographic characteristics, including age, sex, marital status, occupation and educational level attained. The screening visit was followed in two to four weeks by baseline visit. At baseline visit, eligible participants were enrolled to the study groups and baseline blood samples were collected for laboratory analysis as indicated in the study design. Follow-ups were conducted on the HIV-positive patients enrolled into this study at three-monthly Clinic visits in which consultant Physicians carried out a complete clinical examination. During each Clinic visit, the HIV-positive patients were asked about their health status, including questions on the incidence of signs and symptoms of HIV disease (e.g. presence of diarrhoea, oral thrush, wasting and opportunistic infections).

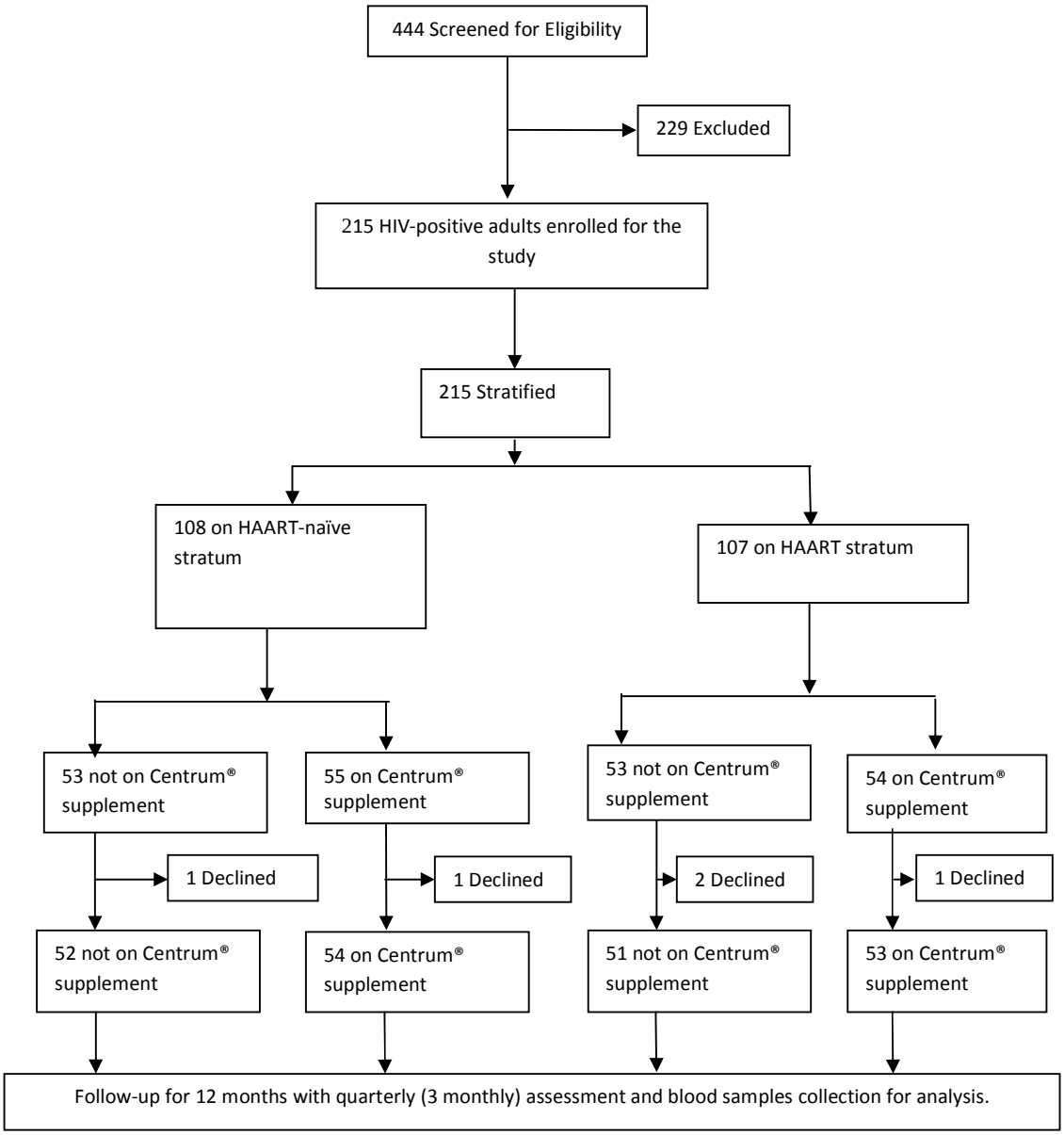

Fig. 1. Study flow chart

2.5 Randomization

The trial flow chart is shown in the Fig. 1. The study regiments were packaged in bottles; prelabeled by the study site Pharmacist with serial numbers according to the study groups. Eligible participants were randomly assigned to micronutrient supplement groups and the control groups using blocked randomization generated by a statistician in blocks of 20. The micronutrient supplement groups received a daily dosage of one RDA of oral multivitamins (A, 3,500 IU; C, 60mg; D3, 400 IU; E, 30 IU; B_1, 1.5 mg; B_2, 1.7 mg; B_6, 2 mg; Niacin, 20 mg; Pantothenic acid, 10 mg; Folic acid, 400 µg and B_{12}, 6 µg) and multimineral (calcium, 162 mg; magnesium, 100 mg; iron, 18 mg; phosphorus, 109 mg; iodine, 150 µg; copper, 2 mg; manganese, 2 mg; potassium, 80 mg; zinc, 15 mg; selenium, 20 µg; chromium, 120 µg and molybdenum, 75 µg) supplement (trade name Centrum®) procured from Pfizer, Madison, NJ 07940, USA and distributed in Nigeria by Pfizer Specialities Limited 38, Opebi road, Adebola House Ikeja, Lagos and control groups received an identical appearing placebo taken as one (1) tablet daily for twelve (12) months. The Centrum® supplement was consumed by the study participants as one tablet daily with meals. The participants were not allowed to use another micronutrient or natural health product. Compliance with the study regimen (Centrum®) was assessed according to the methods of Kupka and co-researchers [29], Kawai and co-workers [30]. The HIV-positive HAART- naïve and HIV-positive patients on HAART that were randomly assigned to the micronutrient supplement (Centrum®) groups, were asked to bring the unused Centrum® tablets back in the next Clinic visit. Participants exchanged a used bottle with a new bottle that contained 100 Centrum® tablets. Compliance with the Centrum® supplement was calculated as the number of Centrum® tablets absent from the returned bottles divided by the total number of Centrum® tablets the subject should have taken and multiplied by 100. This was used as the indicator of the subject's compliance to the study medication.

2.6 Ethical Approval

The study design and protocol were approved by the Ethics and Research Committee of Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto. The research was carried out in accordance with the 1964 declaration of Helsinki concerning the ethical principles for medical research involving human subjects. Written informed consent was obtained from all study participants before enrolment.

2.7 Withdrawal from the Study

Participants were allowed to withdraw from the study at any time and for any reason, or may be withdrawn in the event of intercurrent illness, intolerance to study medication, adverse events, pregnancy, protocol violation or administrative reasons. All participants discontinued due to an adverse event were followed up until the event resolves, or becomes stable and appropriate medical care provided.

2.8 Blood Samples Collection and Processing

Blood samples were collected into sterile plain vacutainer blood specimen bottles from BDH Laboratory supplies, United Kingdom and allowed to clot at room temperature and later centrifuged at 3000 rpm/min for 5 minutes to obtain clear unhaemolyzed serum. The sera were harvested into sterile serum-separation tubes and rapidly stored at -20^{o}C until assayed in batches; for serum activities of antioxidant enzymes and concentrations of MDA.

2.9 Estimation of Biochemical Parameters

Laboratory testing was performed at baseline and every three months for a total of 12 months. Serum SOD activity was estimated as described by Marklund [31] using Superoxide Dismutase Assay Kit procured from Cayman Chemical Company, Ann Arbor, Michigan, USA. The serum CAT activity was estimated by the method of Johansson and Borg [32], using Catalase Assay Kit procured from Cayman Chemical Company, Ann Arbor, Michigan, USA. Serum GPX activity was assayed as described by Paglia and Valentine [33] using Glutathione Peroxidase Assay Kit procured from Cayman Chemical Company, Ann Arbor, Michigan, USA. Serum MDA concentration was estimated by the method of Mihaljevic et al. [34] using Lipid Hydroperoxide (LPO) Assay Kit procured from Cayman Chemical Company, Ann Arbor, Michigan, USA.

2.10 Statistical Analysis

The data obtained were analysed using Microsoft Office® Excel 2007 and Graphpad InStat®

statistical soft ware Version 3.10, 32 Bit for windows (2009). The results were expressed as mean ± SEM. Group comparisons were made using one-way analysis of variance (ANOVA), paired comparisons were carried out using the Student's t-test, and p-value of equal to or less than 0.05 (P≤0.05) was considered as significant.

3. RESULTS AND DISCUSSION

3.1 Results

3.1.1 Enrolment and follow-up

Between April, 2013 and September, 2014, a total of 215 HIV-infected adults were enrolled and stratified into 108 HAART-naïve and 107 HIV-infected on HAART. These were randomized into the study as described by Baum et al. [25] and Guwatudde et al. [35]. The study flow chart is shown in Fig. 1. During the three (3) months follow-up, two participants (2 HAART- naive) and three (3 HIV-infected on HAART) declined to continue with the research. These cases were excluded from the analyses and final computation.

Demographic and HIV-related characteristics of the study population are presented in Table 1. Majority of the HIV-infected patients in the study population are married, predominantly Hausa and most are in CDC stage I of HIV infection.

HIV infection caused significant increase ($p<0.001$) in serum activities of SOD, CAT and GPX (Table 2), and supplementation with micronutrients reversed the trend in HAART-naive HIV-infected patients.

Table 1. Demographic and HIV-related characteristics of the study population

Characteristic	ART-naïve HIV-infected		HIV-infected on HAART	
	Control group (n=52)	Supplement group (n=54)	Control group (n=51)	Supplement group (n=53)
Marital status				
Married	37(71.2%)	36(66.7%)	38(74.5%)	39(73.6%)
Single	10(19.2%)	13(24.1%)	10(19.6%)	10(18.9%)
Widowed	03(5.8%)	04(7.4%)	02(3.9%)	03(5.6%)
Divorced	02(3.8%)	01(1.8%)	01(2.0%)	01(1.9%)
Tribe				
Hausa	34(65.4%)	38(70.4%)	37(72.5%)	38(71.7%)
Fulani	02(3.8%)	02(3.7%)	01(2.0%)	01(1.9%)
Igbo	04(7.7%)	05(9.2%)	04(7.8%)	03(5.7%)
Yoruba	02(3.8%)	02(3.7%)	01(2.0%)	01(1.9%)
Others	10(19.2%)	07(13.0%)	08(15.7%)	10(18.8%)
HIV-related Illness				
Herpes Zoster	04(7.7%)	03(5.6%)	01(2.0%)	01(1.9%)
Kaposi Sarcoma	01(1.9%)	00(0.0%)	01(2.0%)	00(0.0%)
Tuberculosis	07(13.5%)	08(14.8%)	06(11.8%)	08(15.1%)
Opportunistic infection				
Recurrent Diarrhoea	05(9.6%)	03(5.6%)	03(5.9%)	02(3.8%)
Recurrent Typhoid	04(7.7%)	03(5.6%)	03(5.9%)	02(3.8%)
Bronchitis	05(9.6%)	04(7.4%)	03(5.9%)	02(3.8%)
Candidiasis	00(0.0%)	01(1.8%)	02(3.9%)	01(1.9%)
Otitis Media	01(1.9%)	00(0.0%)	01(2.0%)	00(0.0%)
Others	12(23.1%)	14(25.9%)	08(15.7%)	10(18.9%)
Stage of HIV infection				
Stage I	37(71.2%)	36(66.7%)	32(62.7%)	39(73.6%)
Stage II	11(21.1%)	15(27.8%)	16(31.4%)	13(24.5%)
Stage III	03(5.8%)	02(3.7%)	02(3.9%)	01(1.9%)
Stage IV	01(1.9%)	01(1.8%)	01(2.0%)	00(0.0%)

Majority of the HIV-infected patients in the study population are married followed by single, the subjects are predominantly Hausa and most of them in CDC stage I of HIV infection.

Table 2. Effects of micronutrient supplementation on serum activities of superoxide dismutase, catalase and glutathione peroxidase in HAART-Naïve, HIV- infected adults

Parameter	Micronutrient supplement group (n=54)	Control group (n=52)	p-value
SOD (U/ml)			
Baseline	3.11±0.14	3.14±0.29	p>0.05
3 Months	4.02±0.13	2.92±0.25	P>0.05
6 Months	4.96±0.12	2.42±0.18	P<0.001
9 Months	5.86±0.11	2.02±0.14	P<0.001
12 Months	6.24±0.10	1.78±0.13	P<0.001
CAT (nmol/min/ml)			
Baseline	36.94±1.37	36.66±1.41	p>0.05
3 Months	40.91±1.37	34.54±1.41	P<0.001
6 Months	43.88±1.37	31.41±1.43	P<0.001
9 Months	48.71±1.42	27.29±1.47	P<0.001
12 Months	50.96±1.32	28.85±1.48	P<0.001
GPX (nmol/min/ml)			
Baseline	7.78±0.46	8.37±0.47	p>0.05
3 Months	8.96±0.39	7.84±0.33	p>0.05
6 Months	13.25±0.36	7.04±0.23	P<0.001
9 Months	16.65±0.41	5.92±0.20	P<0.001
12 Months	18.42±0.32	4.31±0.20	P<0.001

Values are mean ± SEM; n=number of Subjects, SOD= superoxide dismutase, CAT= catalase and GPX= glutathione peroxidase by independent sample t-test.

The result of effects of micronutrients supplementation on serum activities of SOD, CAT and GPX in HIV-infected patients on HAART is presented in Table 3. The result indicated that supplementation with micronutrients at 6 to 12 months increased significantly (p<0.001) the activities of SOD, CAT and GPX as compared with HIV-infected control.

Table 3. Effects of micronutrient supplementation on serum activities of superoxide dismutase, catalase and glutathione peroxidase in HIV-infected adults on HAART

Parameter	Micronutrient supplement group (n=53)	Control group (n=51)	p-value
SOD (U/ml)			
Baseline	3.23±0.17	3.26±0.34	p>0.05
3 Months	3.78±0.17	2.96±0.28	P>0.05
6 Months	4.25±0.16	2.66±0.25	P<0.001
9 Months	4.68±0.16	1.98±0.25	P<0.001
12 Months	5.78±0.14	1.50±0.23	P<0.001
CAT (nmol/min/ml)			
Baseline	33.53±1.24	35.38±1.33	p>0.05
3 Months	37.50±1.24	33.54±1.33	P<0.001
6 Months	40.53±1.28	26.45±1.33	P<0.001
9 Months	45.86±1.37	20.08±1.33	P<0.001
12 Months	48.34±1.32	18.89±1.24	P<0.001
GPX (nmol/min/ml)			
Baseline	7.50±0.57	7.74±0.61	p>0.05
3 Months	7.50±0.57	7.04±0.47	p>0.05
6 Months	9.34±0.57	6.29±0.31	P<0.001
9 Months	10.81±0.62	5.34±0.27	P<0.001
12 Months	12.68±0.38	4.69±0.21	P<0.001

Values are mean ± SEM; n=number of Subjects, SOD= superoxide dismutase, CAT= catalase and GPX= glutathione peroxidase by independent sample t-test.

Effects of micronutrients supplementation on serum MDA in HAART-naive HIV-infected patients are presented in Table 4. The result indicated significant decrease ($p<0.001$) in the serum level of MDA as compared with the unsupplemented HIV-infected control.

Effects of micronutrients supplementation on serum concentration of MDA in HIV-infected patients on HAART is presented are presented in Table 5. Micronutrients supplementation decreased MDA significantly ($p<0.001$) as compared to the unsupplemented HIV-infected control.

3.2 Discussion

This study reports that at 6 to 12 months follow up the mean serum activities of SOD, CAT and GPX in HAART-naïve HIV–infected and HIV-infected patients on HAART supplemented with micronutrients increased significantly compared with the unsupplemented control groups (Tables 2-3). This is in conformity with the studies of Jaruga et al. [5] who reported decreased serum activities of SOD, CAT and GPX in HIV-infected patients at baseline. It is possible that the low antioxidant enzymes activities is due to either increased utilization of the enzymes in response to the excessive amount of reactive oxygen species (ROS) production or decreased synthesis of the enzymes that may accompany HIV infection. In contrast to the findings in present study, Trotti et al. [36] and Stephensen et al. [37] reported significantly increased erythrocyte GPX activities in HIV-infected subjects which were attributed to an increase in oxidative stress during erythropoesis and subsequently stimulating GPX-1 expression.

Our result corroborated with the previous studies of Gill et al. [38] who reported an increased activity of erythrocyte SOD in HIV-infected patients on HAART supplemented with micronutrients, Muhammad et al. [39] demonstrated that, supplementation with antioxidant minerals resulted to increased activities of CAT, SOD and GPX in salt-induced hypertensive rats compared with controls. Our results were also similar with the findings of Jaruga et al. [5] who reported that, supplementation with antioxidant vitamins (A, C, and E) in HIV-infected patients restored the activities of CAT and SOD compared with controls and Delmas-Beauvieux et al. [40] who reported increased activities of SOD in HIV-infected patients supplemented with selenium.

Table 4. Effects of micronutrient supplementation on serum malondialdehyde concentrations in HAART-Naïve, HIV-infected adults

Parameter	Micronutrient supplement group (n=54)	Control Group (n=52)	p-value
MDA (µl)			
Baseline	29.71±0.62	23.79±0.55	P<0.001
3 Months	28.04±0.62	24.88±0.55	P<0.001
6 Months	24.71±0.62	28.23±0.56	P<0.001
9 Months	16.44±0.63	29.77±0.59	P<0.001
12 Months	14.16±0.64	30.63±0.56	P<0.001

Values are mean ± SEM; n=number of Subjects, MDA=malondialdehyde concentration by independent sample t-test

Table 5. Effects of micronutrient supplementation on serum malondialdehyde concentrations in HIV-infected adults on HAART

Parameter	Micronutrient supplement group	Control group	p-value
MDA (µl)			
Baseline	34.41±0.72	31.40±0.70	P<0.001
3 Months	32.84±0.71	33.10±0.68	P>0.05
6 Months	29.55±0.74	34.70±0.61	P<0.001
9 Months	29.49±0.80	39.37±0.62	P<0.001
12 Months	17.29±0.77	40.20±0.58	P<0.001

Values are mean ± SEM; n=number of Subjects, MDA=malondialdehyde concentration by independent sample t-test

The hallmark of oxidative stress is lipid peroxidation where reactive oxygen species react with the double bonds of polyunsaturated fatty acids of lipids generating relatively unstable lipid peroxides that have the potential to cause cell death [41]. In the current study, there were significant elevations ($p<0.001$) of serum levels MDA in HAART-naïve HIV-infected and HIV-infected patients on HAART unsupplemented with micronutrients (controls) compared with HAART-naïve HIV-infected and HIV-infected patients on HAART supplemented with micronutrients (Tables 4-5). This is consistent with the previous studies [39,42-43] that reported significant increase in oxidative stress in HIV-positive patients as evidenced by increased lipid peroxidation products. Ngondi et al. [44] in their studies also observed an increased oxidative stress in HIV-infected patients in Cameroon as evidenced by significantly increased thiobarbituric acid reducing substances (TBARS) a marker for lipid peroxidation in patients infected with HIV.

In the present study, micronutrient supplementation caused significantly ($p<0.001$) decreased serum concentrations of MDA in HAART-naïve HIV-infected and HIV-infected patients on HAART compared with a relative increase in MDA in the non supplemented groups. This is in agreement with the studies of Allard et al. [21] who reported significant decreases in breath pentane output, plasma MDA and lipid peroxides in HIV-positive subjects after three (3) months of micronutrient supplementation compared with the non-supplemented groups. Our result however indicated that the decreases in serum MDA concentrations were more pronounced in HAART-naïve HIV-infected than HIV-infected patients on HAART. This could be attributed to the increased oxidative stress which was more marked in HIV-positive patients on HAART. This is consistent with reports that HIV-infected patients on HAART are oxidatively stressed as evidenced by significantly increased thiobarbituric acid reducing substances (TBARS) or lipid peroxidation, which was further enhanced by the use of antiretroviral therapy [44].

Our earlier report of the effects of micronutrient supplementation on $CD4^+$ cell count and anthropometric parameters in HIV-positive patients and controls at baseline, 3, 6, 9, and 12 months demonstrates that $CD4^+$ cell count, body weight, and body mass index were lower in HAART-naïve HIV-infected and HIV-infected patients on HAART at baseline and micronutrient supplementation significantly improved $CD4^+$ cell count reconstitution and body mass index of the subjects [45].

4. CONCLUSION

The results in the current study demonstrate that the lower serum activities of antioxidant enzymes and higher lipid peroxidation in HIV-infected HAART-naïve and HIV-infected patients on HAART at baseline were reversed by micronutrients supplementation of the subjects.

5. RECOMMENDATION

The micronutrient supplement used was tolerated and when given at nutritional doses, is likely to reduce oxidative stress and may slow the HIV-disease progression and prolong the time before initiation of ART or used as an adjuvant therapy with HAART. This could reduce the morbidity and mortality in the affected HIV/AIDS patients.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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