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Effects of Micronutrient Supplementation on CD4$^+$ Cell Count and Anthropometric Parameters in HIV-Positive Adults on Highly Active Antiretroviral Therapy and Treatment Naïve 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 and CHN 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 CD4$^+$ cell count and anthropometric parameters in 210 HIV-positive adult patients on highly active antiretroviral therapy and treatment naïve.
Study Design: A prospective and interventional study was performed comparing five groups receiving daily either a micronutrients (Centrum) supplement or no supplement for 12 months, and the effects of micronutrients supplementation on CD4$^+$ cell count and anthropometric parameters 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 Danfodiyo University, Sokoto, between April, 2013 and September, 2014.

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Methodology: We included 210 patients (94 men, 116 women; age range 18-50 years 106 HIV^+ HAART-naïve, 104 HIV^+ on HAART) with HIV infection and 42 gender, age-and socioeconomically-matched HIV-negative controls. Clinical examination as well as laboratory analysis ($CD4^+$ cell count) and anthropometric parameters (weight and height) were measured using standard techniques at baseline and measurement repeated at 3-monthly period for a total of 12 months. Body mass index was calculated using the expression: BMI (kg/m^2) = Body Weight (kg)/Height (m^2).

Results: The results showed that, $CD4^+$ cell count in HIV-positive HAART-naïve (group B and; 514.65±10.45 and 542.91±21.60 cells/µl respectively) and HIV-positive patients on HAART (group D and E; 655.86±34.62 and 594.77±30.89 cells/µl respectively) were significantly ($p<0.001$) lower than the corresponding results among age- and gender–matched controls (group A; 952.02±39.15 cells/µl) at baseline. Mean $CD4^+$ cell count, body weight and body mass index increased significantly ($p<0.001$) in HIV-positive HAART-naïve and HIV-positive patients on HAART that received micronutrients supplement respectively compared to unsupplemented groups.

Conclusion: The results in the current study demonstrates that, the $CD4^+$ cell count, body weight, and body mass index were lower in HIV-positive HAART-naïve and HIV-positive on HAART patients at baseline and micronutrient supplementation significantly improved $CD4^+$ cell count reconstitution and body mass index of the subjects.

Recommendation: The micronutrient supplement used was tolerated and when given at nutritional doses, is likely to improve the immune reconstitution in HIV-positive HAART-naïve and HIV-positive on HAART patients 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; $CD4^+$; HIV; anthropometric parameters; micronutrient supplementation; Nigeria.

1. INTRODUCTION

Infection with human immunodeficiency virus (HIV) is associated with a decline in immunity or the inability to fight infection 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].

Human Immunodeficiency Virus (HIV) infection induces a wide array of immunological alterations resulting in the progressive development of opportunistic infections and malignancy, which results in acquired immunodeficiency syndrome (AIDS). Contributing to this progression, oxidative stress induced by the production of reactive oxygen species (ROS) may play a critical role in the stimulation of HIV replication and the development of immunodeficiency [3]. Moreover, enhanced oxidative stress may be involved in the pathogenesis of impaired T-Cell responsiveness and enhanced T-cell apoptosis during HIV infection, and it may also play a role in the development of certain HIV-related clinical disorders, including malignancies and HIV-related encephalopathy [4].

Studies have demonstrated that HIV-infected individuals, particularly those with advanced disease have enhanced oxidative DNA damage in CD_4^+ T-cells, as assessed by increased 7,8–dihydro-8-oxoguanine (8-oxo-G) accumulation with a marked decline in DNA glycosylase activity, an enzyme necessary for the repair of oxidative base lesion in CD_4^+ T-cells [5]. The increased activity of inflammatory cytokine, tumour necrosis factor-α (TNF-α) and altered intracellular glutathione redox status found in HIV-infected patients may be responsible for promoting oxidative DNA damage in $CD4^+$ T-cells.

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 [6-10]. Adequate nutritional status supports immunity and physical performance, while malnutrition especially through its negative effects on the immune

system, further aggravates HIV infection by increasing the risk of opportunistic infection and death. In turn, HIV-infected persons are at higher risk for malnutrition, and certain conditions can magnify the risk such as anorexia, difficulty in swallowing, malabsorption and diarrhoea, altered metabolism of nutrients, increased utilization of nutrients, and greater loss of nutrients [1].

Because of the essential role of micronutrients in supporting the body's functions, HIV- infected people very much need to have 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. Micronutrient supplementation could be a relatively low cost strategy to defer the initiation of expensive, potentially toxic and lifelong antiretroviral therapy. The current study is therefore aimed at assessing whether micronutrient supplementation of HIV-positive HAART-naïve and those on treatment with HAART, using a micronutrient tablet (Centrum®) could improve the $CD4^+$ cell count and anthropometric parameters in these patients compared with un-supplemented groups.

2. MATERIALS AND METHODS

2.1 Study Subjects and Study Site

Enrolment took place between April, 2012 and September, 2013 at the Antiretroviral Therapy Clinic, Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria. A total of two hundred and ten (210) HIV-infected outpatients with baseline $CD4^+$ cell counts equal to or above 350µl, who were not receiving highly active anti-retroviral drugs (106) and those on treatment with HAART (104), were randomized into Groups B and C; D and E respectively. Groups C and E patients received micronutrient supplements containing 23 nutrients, while those in Groups B and C were not given the supplements. Group A are the controls which comprised of 42 adult persons, sex-and age-and socioeconomic-matched HIV-negative (apparently healthy) individuals and were of the same socioeconomic and demographic characteristics as the patients studied. Group A were also not given the micronutrient supplements.

Eligibility criteria for the patients were; asymptomatic HIV-positive adults who are HAART-naive and HIV-positive adults who are on HAART, both with screening $CD4^+$ T lymphocytes ≥ 350 cells/µl. In all the patients and controls, informed consent was obtained from each prior to the commencement of the study. Study subjects were ineligible if they have allergy or intolerance to any study ingredient, be pregnant, have ALT greater than three times normal range, have known liver cirrhosis, have serum creatinine >133 µmol/l, smoke cigarette, abuse alcohol or be taking micronutrient or natural health product.

2.2 Study Design

The study was a prospective, interventional study where consenting eligible HIV-positive male and female patients Attending Antiretroviral Therapy Clinic, Usmanu University Teaching Hospital, Sokoto were enrolled to receive a micronutrients supplement (Centrum®) or no supplement for 12 months, and the effects of micronutrients supplementation on $CD4^+$ cell count and anthropometric parameters from baseline to 12 months were assessed according to the method described by Hammer et al. [13]. 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 [14].

At enrolment a structured interviewer-administered questionnaire was administered to each patient and information on patient's demographic and socioeconomic characteristics including sex, age, marital status, occupation and education were obtained. Eligible subjects were assigned to the following groups:

Group A (n=42):	HIV-negative controls not supplemented with Centrum®.
Group B (n=53):	HIV-positive HAART-naïve not supplemented with Centrum®.
Group C (n=55):	HIV-positive HAART-naïve supplemented with Centrum®.

Group D (n=53): HIV-positive on HAART not supplemented with Centrum®.
Group E (n=54): HIV-positive on HAART supplemented with Centrum®.

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 [15].

2.3 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.

2.4 Study Regimen

The study regimen used was a commercially formulated micronutrient supplement that included 23 ingredients with a 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. The subjects were randomly assigned to receive micronutrient supplement (Centrum® tablet) or not receive the micronutrient supplement (Centrum® tablet) for 12 months. The Centrum® 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 [16], Kawai and co-workers [17]. 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.

2.5 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.

2.6 Screening, Baseline, and Follow-up Assessments

All the HIV-positive patients were consecutively selected from the population of HIV positive patients Attending Antiretroviral Therapy Clinic (ART Clinic), Usmanu Danfodiyo University Teaching Hospital Sokoto. Potential participants were identified by preliminary screening at routine Clinic visits. At the ART Clinic, HIV-positive patients who satisfied the study inclusion criteria were consecutively selected until the desired sample size was attained. All the patients were evaluated by the consultant Physicians at the Clinic. 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 3-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). The clinical assessment incorporated self-administered patient questionnaires. The linear analogue self assessment tool assessed the patient's energy level, ability to perform daily activities and overall quality of life on a linear scale.

2.7 Blood Samples Collection and Processing

From each selected subject, a total of three millilitres (3.0 ml) of venous blood specimen was collected using a sterile EDTA vacutainer blood specimen bottles, holder and needle.

2.8 Enumeration of $CD4^+$ Cell Count

The $CD4^+$ cell was enumerated at baseline and every three (3) months for a total of 12 months. The $CD4^+$ cells were enumerated by flow cytometry (FCM) method of Cassens et al. [18], using Cyflow Counter manufactured by Partec, Munster, Germany.

2.9 Measurement of Anthropometric Parameters

Anthropometric parameters were measured at baseline and every three (3) months for a total of 12 months using standard techniques. Subjects were weighted with minimum clothing to the nearest 0.1 kg by using a regularly calibrated weighing health scale; model ZT 120 (manufactured by Seca Gmbh and Co., Germany), while the heights were measured by using a calibrated Stadiometer, model 220 (manufactured by Seca Gmbh and Co., Germany). Body mass index (BMI) for each subject was calculated using the following formula: BMI (kg/m^2) = Body Weight (kg)/Height (m^2).

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 ($P \leq 0.05$) was considered as significant.

3. RESULTS AND DISCUSSION

3.1 Results

The demographic and HIV-related characteristics of the study population were shown in Table 1. Majority of the HIV-infected patients in the study population are married (71.1%) followed by single (20.6%), the subjects are predominantly Hausa and most of them in CDC stage I (56.7%) of HIV infection. The effect of sex on CD_4^+ cell count and anthropometric parameters in HIV-positive patients and controls was presented in Table 2. The differences in the mean age, height, BMI and CD_4^+ cell count were statistically significant ($P < .001$) with mean age and height higher in HIV-positive male patients while mean BMI and CD_4^+ cell count higher in female HIV-positive patients (Table 2). It should be noted that in the course of follow-ups during the research some of the patients declined to continue with the research while others absconded. These cases were excluded from the analysis and final computation.

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

Characteristic	Number of subjects	Percentage (%)
Marital status	252	100
Married	180	71.4
Single	52	20.6
Widowed	15	6
Divorced	5	2
Tribe	252	100
Hausa	181	71.8
Fulani	7	2.8
Igbo	19	7.5
Yoruba	5	2
Others	40	15.9
HIV-related Illness	40	15.9
Herpes Zoster	3	1.19
Kaposi Sarcoma	2	0.79
Tuberculosis	35	13.9
Opportunistic infection	89	35.3
Recurrent Diarrhoea	13	6.2
Recurrent Typhoid	12	5.7
Bronchitis	14	6.7
Candidiasis	4	1.9
Otitis Media	2	0.9
Others	44	21
Stage of HIV infection	210	83.3
Stage I	143	56.7
Stage II	56	22.2
Stage III	8	3.2
Stage IV	3	1.2

The Effects of micronutrient supplementation on CD_4^+ cell count and anthropometric parameters in HIV-positive patients and controls at baseline, 3, 6, 9, and 12 months post supplementation were presented in Table 3. The mean $CD4^+$ cell count in HIV–positive HAART-naïve patients (group B and group C) (514.65±10.45 cells/µl and 542.91±21.60 cells/µl respectively) and HIV–positive on HAART patients (group D and group E) (655.86±34.62 cells/µl and 594.77±30.89

cells/µl respectively) were significantly (P< .001) lower than the corresponding values in controls (952.02±39.15 cells/µl) at baseline. Micronutrient supplementation significantly increased mean $CD4^+$ cell count, body weight and body mass index in HIV-positive HAART-naïve and HIV-positive on HAART patients at 9 to 12 and 12 months respectively (Table 3 and Fig. 1).

The distribution of body mass index in HIV-positive patients and controls at baseline was presented in Table 4. Various forms of nutritional status were found among the subjects studied including which ranges from underweight, normal weight, mild, moderate and morbid obesity based on the WHO classification of BMI [19].

Majority of the HIV-infected patients in the study population are married (71.1%) followed by single (20.6%), the subjects are predominantly Hausa and most of them in CDC stage I (56.7%) of HIV infection.

Table 2. Impact of sex on CD_4^+ cell count and anthropometric parameters in HIV-positive patients and controls

Parameter	HIV-negative controls		HIV-positive patients		P value
	Male (n=20)	Female (n=22)	Male (n=94)	Female (n=116)	
CD4 (cells/µl)	927.00±53.06^{c1d1}	974.77±57.84^{c2d2}	544.70±17.60^{a1b1}	602.15±19.42^{a2b2}	P<0.001
Age (years)	30.95±2.30^{c1}	31.32±1.84	36.18±0.85^{ad}	31.82±0.66^{c2}	P<0.001
Body weight (kg)	64.10±2.81	63.30±2.24	65.59±1.31	66.96±1.41	P>0.05
Height (m)	1.59±0.01^{c1}	1.63±0.01^{c2}	1.68±0.01^{ab1d}	1.62±0.01^{c3}	P<0.001
BMI (kg/m^2)	25.16±1.00	23.82±0.78	23.20±0.42^{d}	25.54±0.52^{c}	P<0.001

*Values are mean ± SEM; n=number of Subjects; CD4= cluster of differentiation type 4; BMI=Body Mass Index; there are no statistically Significant differences **a1**(p<0.05)=male controls versus male patients; **a2** (p<0.001)=male controls versus female patients; **b1**(p<0.05) =female controls versus male patients; **b2** (p<0.001)=female controls versus female patients; **c1**(p<0.05)=male patients versus male controls; **c2**(p<0.001)=male patients versus female controls; **c3**(p<0.0.001)=male patients versus female patients; **d1**(p<0.001) =female patients versus male control; **d2**(p<0.001)=female patients versus female controls by Bonferroni multiple comparison test*

Table 3. Effects of micronutrient supplementation on CD_4^+ cell count and anthropometric parameters in HIV-positive patients and controls at baseline, 3, 6, 9, and 12 months post supplementation

Characteristics	Group A (n=42)	Group B (n=52)	Group C (n=54)	Group D (n=51)	Group E (n=53)
CD_4 (cells/µl)					
Baseline	952.02±39.15	514.65±10.45^{a1}	542.91±21.60^{a2}	655.86±34.62^{a3b1c2}	594.77±30.89^{a4}
3 Months	-	506.65±10.45	546.18±22.06	621.84±31.70^{b1c2}	618.40±29.88
6 Months	-	483.10±10.56	574.18±22.06	621.17±30.68^{b1}	633.65±31.06^{b2}
9 Months	-	449.90±10.21^{c1}	604.60±22.62	605.71±31.78^{b1}	667.02±33.44^{b2}
12 Months	-	425.49±10.53^{c1}	643.36±22.65	577.65±31.59^{b1}	694.82±32.84^{b2d}
Body weight (Kg)					
Baseline	63.68±1.76	61.51±1.59	65.18±1.63	68.84±2.08	69.88±2.24^{b2}
3 Months	-	60.48±1.54	67.48±1.60	67.84±2.00^{b1}	70.50±2.22^{b2}
6 Months	-	59.30±1.48^{c1}	70.58±1.55	64.65±1.86^{b1}	71.63±2.30^{b2}
9 Months	-	58.08±1.43^{c1}	73.30±1.60	64.65±1.86^{c2}	72.60±2.60^{b2d}
12 Months	-	55.08±1.28^{c1}	76.95±1.64	62.92±1.86^{b1c2}	75.79±2.39^{b2d}
BMI(Kg/m^2)					
Baseline	24.45±0.63	22.70±0.55	23.98±0.60	25.06±0.73	26.24±0.83^{b2}
3 Months	-	22.33±0.54	24.84±0.59	24.70±0.70	26.56±0.90^{b2}
6 Months	-	21.82±0.53^{c1}	25.99±0.58	24.49±0.65	26.98±0.93^{b2}
9 Months	-	21.26±0.52^{c1}	27.02±0.62	23.53±0.65^{c2}	27.18±1.04^{b2d}
12 Months	-	20.19±0.41^{c1}	28.35±0.64	22.90±0.64^{b1c2}	28.47±0.98^{b2d}

*Values are mean ± SEM; n=number of Subjects; CD4= cluster of differentiation type 4; BMI=Body Mass Index; Significant differences: **a**^{1} (P<0.001) = Control versus Group B; **a**^{2} (P<0.001) = Control versus Group C; **a**^{3} (P<0.001) = Control versus Group D; **a**^{4} (P<0.001) = Control versus Group E; **b**^{1} (P<0.001) = Group B versus Group D; **b**^{2} (P<0.001) = Group B versus Group E; **c**^{1} (P<0.001) = Group C versus Group B; **c**^{2} (P<0.001) Group C versus Group D; **d** (P<0.001) = Group D versus Group E by Bonferroni multiple comparison test*

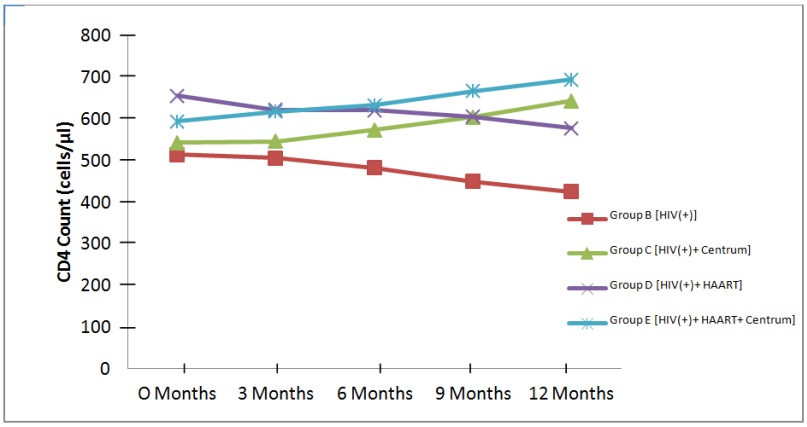

Fig. 1. CD_4^+ Cell count in HIV-Positive patients at baseline, 3, 6, 9 and 12 months Post supplementation with Centrum®

Table 4. Distribution of Body Mass Index (BMI) in the study population

Group	N	Classification of BMI (WHO, 2012)					
		Underweight	Normal weight	Overweight	Mild obesity	Moderate obesity	Morbid obesity
		<18.5 (Kg/m^2)	18.5-24.99 (Kg/m^2)	25-29.99 (Kg/m^2)	30-34.99 (Kg/m^2)	35-39.99 (Kg/m^2)	≥ 40 (Kg/m^2)
A	42	2(4.8%)	20(47.6%)	17(40.5%)	3(7.1%)	-	-
B	52	7(13.5%)	32(61.5%)	11(21.2%)	1(1.9%)	1(1.9%)	-
C	54	5(9.3%)	28(51.9%)	18(33.3%)	2(3.7%)	1(1.9%)	-
D	51	3(5.7%)	23(43.4%)	21(39.6%)	3(5.7%)	2(3.8%)	1(1.9%)
E	53	4(7.5%)	23(43.4%)	14(26.4%)	9(17.0%)	1(1.9%)	2(3.8%)

Values are number of subjects with percentage in parenthesis classified according to nutritional status; n=number of subjects and BMI=Body Mass Index

Key- BMI (kg/m2) Class, Underweight: <18.5, Normal weight: 18.5-24.99, Overweight: 25-29.99, Mild Obesity: 30-34.99, Moderate Obesity: 35-39.99, Morbid Obesity: ≥ 40

3.2 Discussion

The result of this study showed an improved immunological status and well being of the HIV-positive HAART-naïve and HIV-positive on HAART patients as evidenced by the increased $CD4^+$ cell count, body weight and body mass index at 9 to 12 and 12 months post supplementation respectively in HIV–positive HAART-naïve and HIV-positive on HAART patients (Table 4) is consistent with reports of previous studies [8,20-23] who indicated significant increase of $CD4^+$ cell count in HIV-positive subjects supplemented with micronutrients.

This study also demonstrated that, at baseline the differences in mean values of age, height, BMI and CD_4^+ cell count were statistically significant (P<0.001) with mean age and height higher in HIV-positive male patients while mean BMI and CD_4^+cell count higher in female HIV-positive patients. The reason for this could be attributed to the fact that, HIV-positive male patients in the study area were adamant and reluctant to access health care services on time due to psychological fear of being discriminated and stigmatized, hence the observed decrease in body mass index and CD_4^+ cell counts may be associated with wasting and decrease in immune function all of which are determinants of HIV disease progression.

The mechanism by which micronutrient supplementation may increase the $CD4^+$ cell count is not well understood. It is also not possible to clearly define from this study, the specific micronutrient or their combination that is responsible for the observed increase in the $CD4^+$cell count. Supplementation of HIV-infected African women with antioxidant vitamins C, E and B vitamins significantly improved the $CD3^+$, $CD4^+$ and $CD8^+$ cell counts [8].

In addition, the increase in $CD4^+$ cell count after micronutrient supplementation in HIV-infected individuals has previously been described by several researchers [8-9]. A significant decrease

in $CD4^+$ cell apoptosis and reduction of viral load and have also been observed following supplementation of antioxidant micronutrients supplementation [7-8]. The mechanism of apoptosis in HIV-infected CD4 cells is thought to result from the direct effect of HIV itself and from concomitant antioxidant imbalances in host cells [24-25]. In this study, amelioration of the antioxidant imbalances through micronutrient supplementation may lead to a subsequent reduction in the rate of $CD4^+$ cell apoptosis which may account for the increase in $CD4^+$ cell count observed in our study.

4. CONCLUSION

This study demonstrates that a micronutrient supplement (Centrum®) administered at nutritional doses can significantly improve $CD4^+$ cell count, body weight and body mass index in HIV-positive adults on highly active antiretroviral therapy and treatment naïve patients. The Centrum micronutrient supplement used was also tolerated and we therefore support the use of the micronutrient supplement to be used as an adjuvant therapy with HAART for those patients with advanced HIV-disease or may prolong the time before initiation of ART for treatment naïve patients. This could reduce the morbidity and mortality in the affected HIV/AIDS patients.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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