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# Multiple Micronutrient Supplementation Effect on Vital Metabolic parameters of Stable HIV Patients on Long term Highly Active Antiretroviral Therapy; A Randomized Crossover Trial

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**A B S T R A C T**

The effective and widespread use of Highly Active Antiretroviral Therapy (HAART) has resulted in people with Human Immunodeficiency Virus (HIV) infection now living longer especially in resource limited regions with non AIDS defining diseases becoming a major cause of illness and management concern in patients on long term HAART. To determine the effect of multiple micronutrient supplementation on the vital metabolic parameters of clinically stable HIV patients on long term HAART. A randomized crossover intervention trial was used to determine the effect of a 12 week daily consumption of multiple micronutrient supplements on 50 clinically stable HIV infected clients receiving treatment from the Imo State University Teaching Hospital. The participants were purposively selected based on certain inclusion criteria and were randomized into two groups to receive the supplement at different periods after a washout period. The measurements of the levels of the metabolic parameters were taken at baseline, 12, 20 and 32 weeks. The mean age of the participants studied was 43.8±10.8 years with an average duration on HAART of 3.2±1.5 years. At baseline, 55.3% of the participants were severely immunodeficient, 51.1% were either overweight or obese, 45% were hypertensive and 57.4%, 55.3%, 80.9% and 68.1% respectively had high serum urea, albumin and liver enzymes. The intervention result, revealed that there was no statistically significant difference in the levels of the vital metabolic parameters with micronutrient supplementation compared to no supplementation. Micronutrient supplementation in HIV patients on long term HAART appear not to have any significant effect on the vital metabolic parameters.

## Introduction

The effective and widespread use of HAART has resulted in people with HIV infection now living longer as HAART alone has been associated with the halting of the devastation and rapid progression of the disease due to immunodeficiency, wasting, metabolic disorders and nutrient deficiencies (Beach et al., 1992; Montaner et al., 1998).

The clinical consequences of effective and widespread use of HAART has been longer survival and improved quality of life of HIV infected patients with the emergence of non AIDS defining illnesses such as malignancies, cardiovascular, renal, hepatic and other related disorders with its associated abnormal levels of metabolic parameters (Montaner *et al*., 1998; Walensky *et al*.; Wester *et al*., 2011).

The risk of developing non AIDS defining illnesses in HIV patients on long term HAART especially resource poor countries is increasing as more people are now on HAART for longer periods as is the case in the developed countries where treatment with HAART began since 1996 (Panel on Antiretroviral Guidelines for Adults and Adolescents). A Swiss Cohort study observed that while the incidences of AIDS defining events are reducing, the non AIDS defining events are increasing with aging and as a consequence, the non AIDS related diseases are now becoming major causes of health concern in HIV patients on long term HAART with associated morbidity and mortality [Hasse *et al*., 2011; The Antiretroviral Therapy Cohort Collaboration (ART-CC writing committee); 2010]. This particularly appears to be constituting a significant problem in sub Saharan Africa and therefore requires that monitoring, prevention and treatment should be a critical component of care in resource limited regions (Wester *et al*., 2011).

Nutritionappears to play a role in the development of non AIDS defining illnesses in HIV patients on long term HAART as a study by Wester *et al*. (Wester *et al*., 2011) reported an increased incidence of non AIDS defining illnesses in an African Cohort especially among the overweight adults. With HIV and nutrition being strongly related, the nutritional implications in the prognosis and management of HIV infection especially in developing countries is highlighted by the associated prevalence of nutrient deficiencies established early in the course of HIV infection coupled with the fact that micronutrient deficiencies are more likely to occur among residents of developing countries like Nigeria; that is ranked the 3$^{rd}$ highest with respect to absolute numbers of stunting with annual losses of US$1.5 billion in Gross Domestic Product due to vitamins and mineral deficiencies (Montaner *et al*., 1998; United Nations Children's Fund (UNICEF),2009; World Bank; Jiang *et al*., 2012).

It has been established that HIV infection can lead to micronutrient deficiencies and these micronutrient deficiencies may persist in these patients on long term HAART which may in turn affect the absorption, pharmacokinetics and hence toxicity of HAART thereby influencing the levels of their vital metabolic parameters; even though it has been reported that the initiation of HAART may improve some of these deficiencies observed in these patients (Keusch, 1990; Raiten *et al*., 2005).

Similarly, it has been observed that HIV patients on long term HAART have improved nutritional states probably from diet, even though it has also been observed that most of the protective effects of micronutrient consumption were due to intake of supplements rather than diet whichwas correlated to its ability to decrease

oxidative damages and enhance immunity (Baum *et al*., 2013). Furthermore, it has been suggested that micronutrient supplementation may play a role in reducing mitochondrial dysfunction, oxidative stress and metabolic complications which are commonly experienced by HIV patients receiving HAART (Drain *et al*., 2007).

## Methodology

### Study Area

The study was conducted at the adult HIV clinic of Imo State University Teaching Hospital situated in Orlu Local Government Area (LGA) of Imo State, South East, Nigeria. The study area is predominantly rural with a population density varying from 230-1400 persons per sq. km. The HIV clinic has a total enrolment of 4769 patientsand offers comprehensive outpatient HIV care services to about 900 patients monthly, comprising those residing within and outside the State (Iwu *et al*., 2016).

### Study Population

The study population comprised of adult HIV infected patients accessing HAART from the HIV clinic who were either on the first or second line drug regimen consisting of Zidovudine, Lamuvidine, Emtricitabine, Tenofovir, Abacavir Nevirapine, Efavirenz, Atazanavir and Lopinavir/Ritonavir.

### Study Design

The study design was a randomized single blinded controlled AB/BA crossover interventional trial. The study participants were randomized into two groups AB and BA. The AB received micronutrient supplement and BA received no supplement in the first intervention period (0-12 weeks), following a washout period of 8 weeks, the groups were crossed over with the BA group subsequently receiving micronutrient supplement and AB receiving no supplement in the second intervention period (20-32 weeks).

### Study Intervention Product

The study intervention product was a multiple micronutrient supplement which is commercially available as Immunance tablets and developed by Meyer/Vitabiotics of Meyer health care PVT Ltd. The tablets were taken once daily for 12 weeks. Drug constituents are shown below;

### Sample Size/Sample Technique

The minimum sample size of 15 participants per group was calculated using the approximate approach and in anticipation of a possible significant carryover effect which may necessitate the setting aside of the second treatment period data in order to analyse only the first treatment period; the researchers increased the total number of participants in the study to 50 to accommodate this possibility. The fifty participants were selected using purposive sampling technique based on certain inclusion and exclusion criteria but 3 participants were lost to follow up (AB group=25and BA group=22).

### Selection Criteria

The selection criteria were based on the following; having CD4 T cell counts of 350 cells/ul or less, receiving HAART for at least one year, with a minimum clinic attendance of 95% and were clinically stable i.e. having no fever, diarrhoea or cough. Patients on current or previous micronutrient supplement use within the last three months, pregnant women or women intending to get pregnant, breastfeeding mothers were excluded from the study.

## Clinical/Laboratory Measurements

All clinical measurements such as weight, height and blood pressure were done using standard measurement scales and blood pressure apparatus by the nursing officers. The laboratory measurements of the metabolic parameters which included serum cholesterol, serum albumin, serum creatinine, serum urea, serum alkaline phosphatase, random blood sugar and liver enzymes i.e.serum glutamic oxaloacetic transaminase (SGOT)and serum glutamic-pyruvic transaminase (SGPT) were done by the principal medical laboratory scientist and assisted by medical laboratory technicians using Randox diagnostic reagent Kits. The laboratory established its own reference range with guidance of the Randox kit expected normal values to reflect the age, sex, diet and geographical location of the population. Laboratory reference for normal values as shown in Figure 2.

## Data Analysis

The data collected from the AB/BA groups were analysed with SPSS version 20 and compared using Independent sample t test with a two sided hypothesis and a p-value set at 0.05. In analysing the intervention effect on metabolic parameters, the mean of the within subject differences of the levels of the particular metabolic parameter of the AB group at 12 and 32 weeks were compared with the mean of the within subject differences of thatmetabolic parameter of the BA group at 12 and 32 weeks. In analysing for carryover effects, the mean of the within subject sums of the levels of the particular metabolic parameterof the AB group at 12 and 32 weeks were compared with the mean of the within subject sums of that metabolic parameter of the BA group at 12 and 32 weeks.

## Ethical Approval

Ethical approval was obtained from the Ethics Committee of Imo State University Teaching Hospital (IMSUTHEC) and written informed consents were obtained from the participants. All authors hereby declare that the study has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

## Limitations of Study

The study assessed the effect of multiple micronutrient supplementation in clinically stable HIV patients on long term HAART and not on HAART naïve patients with obvious signs and symptoms of acute disease. Furthermore, the sample size determination was based on achieving a minimum treatment difference of 12 cells/mm$^3$ in the levels of CD4 T Cell count. Based on these, caution should be taken in generalizing the findings of this work.

## Results and Discussion

Fifty participants were recruited to the study but three participants dropped out from the study after randomization with the AB and BA groups having 25 and 22 participants respectively. The two groups were similar with respect to their socio-demographic characteristics. More than half of the participants were females (55.7%), married (53.2%) and were traders (57.4%) with majority of the participants (70.3%) being within the ages of 30-49 years old and having either a primary or secondary school education as their highest level of educational status (89.4%). The average number of years the participants were on HAART was 3.2±1.3 years with the majority (85.1%) receiving Zidovudine, Lamivudine and Nevirapine combination therapy. There was no statistically

significant difference in socio-demographic characteristics of the groups, p>0.05. Table 1.

At baseline the two groups were similar with respect to CD4 T cell counts, Body Mass Index and Blood Pressure measurements. More than half of the participants were severely immunodeficient, (55.3%) and were either overweight or obese, (51.1%). About 44.7% of the participants had high blood pressure measurements (Table 2).

The two groups AB and BA were similar with respect to the baseline vital metabolic parameters (p>0.05) except for serum cholesterol levels (p=0.005). At baseline, more than three quarters of the participants had normal serum cholesterol levels (87.2%), normal serum creatinine levels (93.6%) and high serum GOT levels (80.9%) with more than half of the participants having high serum albumin levels (55.3%), high serum GPT levels (68.1%), high serum urea levels (57.4%) and normal random blood sugar levels (55.3%). Table 3.

At 12 weeks after supplementation of the AB group, there was no statistical significant difference in each of the following mean metabolic parameters (serum GPT, GOT, Alkaline Phosphatase, Albumin) between the AB and BA groups. (p>0.05) At 32 weeks after supplementation of the BA group, there was no statistical significant difference in each of the mean metabolic parameters (serum GPT, GOT, Alkaline Phosphatase, Albumin)between the AB and BA groups. (p>0.05) Overall, the mean ofwithin subject differences between the $12^{th}$ and $32^{nd}$ week for each metabolic parameter of the AB group did not differ significantly from the mean of within subject differences of the BA group of the corresponding metabolic parameter. (p>0.05)Also the within subject sums between the $12^{th}$ and $32^{nd}$ week of the ABgroup for each metabolic parameter did not differ significantly from the within subject sums of the corresponding metabolic parameter in the BA group. (p=0.05). Table 4.

At 12 weeks after supplementation of the AB group, there was no statistical significant difference in each of the following mean metabolic parameters (serum Cholesterol, Urea, Creatinine and Random blood sugar) between the AB and BA groups. (p>0.05) At 32 weeks after supplementation of the BA group, there was no statistical significant difference in each of the mean metabolic parameters (serum Cholesterol, Urea, Creatinine and Random blood sugar) between the AB and BA groups. (p>0.05) Overall, the mean of within subject differences between the $12^{th}$ and $32^{nd}$ week for each metabolic parameter of the AB group did not differ significantly from the mean of within subject differences of the BA group of the corresponding metabolic parameter. (p>0.05)Also the within subject sums between the $12^{th}$ and $32^{nd}$ week of the AB group for each metabolic parameter did not differ significantly from the within subject sums of the corresponding metabolic parameter in the BA group. (p=0.05). Table 5.

Using the analytical approach of crossover designs based on the publication by Wellek *et al*, [17]the results suggest that multiple micronutrient supplementation did not have any statistically significant effect on the levels of the vital metabolic parameters (serum cholesterol, serum albumin, serum creatinine, serum urea, serum alkaline phosphatase, random blood sugar, SGOT and SGPT) in HIV patients on long term HAART. According to Wellek *et al*., the consideration is that the two randomized groups within the sample are independent since each group receives supplementation at different intervention periods i.e. 0-$12^{th}$ week for the AB group and $20^{th}$-$32^{nd}$ week

for the BA group after a washout period. This results inone group receiving supplements while the other group does not receive any supplementin that particular intervention period. So in effect the participants who received supplements in the first intervention period, did not receive in the second intervention period and the group means (AB, BA) of the differences (within subject differences) in the levels of the metabolic parameters for each participant between the 12th and 32nd week were compared.

## **Table.1** Distribution of Sociodemographic Characteristics

**Table 1: Distribution of Sociodemographic Characteristics**

| | A-B Grp (n=25) Freq | B-A Grp (n=22) Freq | Total(%) | Statistic | df | p-value |
|---|---|---|---|---|---|---|
| **Age(Yrs)** | | | | | | |
| 30-39 | 9 | 11 | 20(42.6) | t=1.96 | 45 | 0.057 |
| 40-49 | 6 | 7 | 13(27.7) | | | |
| 50-59 | 4 | 3 | 7(14.9) | | | |
| 60-69 | 6 | 1 | 7(14.9) | | | |
| X±SD | 46.6±11.5 | 40.6±9.1 | 43.8±10.8 | | | |
| **Gender** | | | | | | |
| Male | 12 | 9 | 21(44.7) | $\chi2$ =0.24 | 1 | 0.626 |
| Female | 13 | 13 | 26(55.3) | | | |
| **Occupation** | | | | | | |
| Trading | 13 | 14 | 27(57.4) | $\chi2$ =0.88 | 3 | 0.831* |
| Business | 7 4 | | 11(23.4) | | | |
| Artisan | 3 | 2 | 5(10.6) | | | |
| Civil Servant | 2 | 2 | 4(8.5) | | | |
| **MaritalStatus** | | | | | | |
| Single | 1 | 6 | 7(14.9) | $\chi2$ =5.38 | 2 | 0.068* |
| Married | 15 | 10 | 25(53.2) | | | |
| Separated | 9 | 6 | 15(31.9) | | | |
| **Education** | | | | | | |
| Primary | 14 | 7 | 21(44.7) | $\chi2$ =3.59 | 1 | 0.166* |
| Secondary | 8 | 13 | 21(44.7) | | | |
| Tertiary | 3 | 2 | 5(10.6) | | | |
| **Years HAART** | | | | | | |
| 1-2 | 11 | 8 | 19(40.4) | t=1.25 | 45 | 0.218 |
| 3-4 | 11 | 7 | 18(38.3) | | | |
| 5-6 | 3 | 7 | 10(21.3) | | | |
| X±SD | 3.0±1.3 | 3.5±1.7 | 3.2±1.5 | | | |

***Likelihood ratio used when >20% cells have expected values <5**

## **Table.2** Distribution of Baseline CD4 and Physical Parameters

**Table 2: Distribution of baseline CD4 and Physical Parameters**

| | A-B Grp (n=25) Freq | B-A Grp (n=22) Freq | Total(%) | Statistic | df | p-value |
|---|---|---|---|---|---|---|
| **CD4(1) cells/ul** | | | | | | |
| ≤350>200 | 11 | 10 | 21(44.7) | t=0.93 | 36 | 0.360 |
| ≤20014 | 12 | 26(55.3) | | | | |
| X±SD | 182.4±63.6 | 204.8±96.6 | 192.9±80.6 | | | |
| **Blood Pressure(2)** | | | | | | |
| Normal | 14 | 12 | 26(55.3) | $\chi2$ =0.01 | 1 | 0.920 |
| High | 11 | 10 | 21(44.7) | | | |
| **BMI(3) kg/m$^2$** | | | | | | |
| 18.5-25.0 | 14 | 9 | 23(48.9) | t=2.95 | 45 | 0.769 |
| >25- 29.9 | 7 | 10 | 17(36.2) | | | |
| >30 | 4 | 3 | 7(14.9) | | | |
| X±SD | 24.8±4.3 | 25.2±3.9 | 25.0±4.1 | | | |

(1) Advanced Immunodeficiency- CD4 T cells≤350 but>200mm$^3$, Severe Immunodeficiency-CD4 T cells≤200mm$^3$ (2) Systolic and Diastolic taken into account (3) Normal BMI- 18.5-25.0 kg/m$^2$

## **Table.3** Distribution of Baseline Vital Metabolic Parameters

**Table 3 Distribution of baseline Vital Metabolic Parameters**

| | | A-B Grp(n=25) Freq | B-A Grp(n=22) Freq | Total(%) | Statistic | df | pvalue |
|---|---|---|---|---|---|---|---|
| Cholesterol | Low | 4 | 1 | 5(10.6) | t=2.93 | 45 | **0.005** |
| | Normal | 21 | 20 | 41(87.2) | | | |
| | High | 0 | 1 | 5(2.1) | | | |
| | Mean±SD | 3.3±0.8 | 4.1±1.1 | 3.6±1.0 | | | |
| Albumin | Low | 2 | 2 | 4(8.5) | t=0.05 | 45 | 0.963 |
| | Normal | 11 | 6 | 17(36.2) | | | |
| | High | 12 | 14 | 26(55.3) | | | |
| | Mean±SD | 42.9±4.3 | 42.8±4.7 | 42.9±4.4 | | | |
| Alk Phos | Normal | 19 | 15 | 34(72.3) | t=0.27 | 45 | 0.786 |
| | High | 6 | 7 | 13(27.7) | | | |
| | Mean±SD | 30.2±12.4 | 31.1±10.9 | 30.6±11.6 | | | |
| Serum GOT | Normal | 5 | 4 | 9(19.1) | t=1.85 | 45 | 0.071 |
| | High | 20 | 18 | 38(80.9) | | | |
| | Mean±SD | 22.0±12.7 | 31.3±21.4 | 26.3±17.7 | | | |
| Serum GPT | Normal | 8 | 7 | 15(31.9) | t=0.72 | 45 | 0.478 |
| | High | 17 | 15 | 32(68.1) | | | |
| | Mean±SD | 18.8±9.8 | 21.1±12.6 | 19.9±11.1 | | | |
| Serum Urea | Low | 0 | 3 | 3(6.4) | t=0.59 | 45 | 0.556 |
| | Normal | 12 | 5 | 17(36.2) | | | |
| | High | 13 | 14 | 27(57.4) | | | |
| | Mean±SD | 7.6±3.4 | 8.3±4.6 | 7.9±4.0 | | | |
| Serum Creat | Normal | 23 | 21 | 44(93.6) | t=0.49 | 45 | 0.625 |
| | High | 2 | 1 | 3(6.4) | | | |
| | Mean±SD | 86.1±30.2 | 81.9±28.3 | 84.1±29.1 | | | |
| R Bld Sugar | Low | 8 | 12 | 20(42.6) | t=0.25 | 34 | 0.807 |
| | Normal | 17 | 9 | 26(55.3) | | | |
| | High | 0 | 1 | 1(2.1) | | | |
| | Mean±SD | 3.8±1.3 | 3.7±2.1 | 3.8±1.7 | | | |

## **Table.4** Distribution of Mean Serumlevels of GPT, GOT, Alkaline Phosphatase, Albumin

**Table 4 Distribution of mean serumlevels of GPT, GOT, Alkaline phosphatase, Albumin**

| | AB Grp (n=25) | BA Grp (n=22) | t | df | p-value |
|---|---|---|---|---|---|
| **SGPT(U/L)** | | | | | |
| 12wks | 14.4±10.5 | 16.0±9.6 | -0.53 | 45 | 0.599 |
| 32wks | 14.2±10.2 | 14.9±7.1 | -0.27 | 45 | 0.786 |
| 12/32wks | | | | | |
| *Within sub diff | 0.2±4.6 | 1.1±5.0 | -0.60 | 45 | 0.550 |
| 12/32wk | | | | | |
| **Within sub sum | 28.6±20.2 | 30.9±16.1 | -0.42 | 45 | 0.675 |
| **SGOT(U/L)** | | | | | |
| 12wks | 18.3±12.0 | 23.1±13.5 | -1.27 | 45 | 0.210 |
| 32wks | 18.0±10.1 | 20.9±11.4 | -0.90 | 45 | 0.372 |
| 12/32wks | | | | | |
| *Within sub diff | 0.3±5.4 | 2.2±5.9 | -1.15 | 45 | 0.256 |
| 12/32wks | | | | | |
| **Within sub sum | 36.4±21.4 | 43.9±24.3 | -1.13 | 45 | 0.264 |
| **Alka phos(IU/L)** | | | | | |
| 12wks | 23.1±7.5 | 25.4±6.7 | -1.12 | 45 | 0.268 |
| 32wks | 24.5±6.7 | 25,5±6.6 | -0.50 | 45 | 0.617 |
| 12/32wks | | | | | |
| *Within sub diff | -1.4±5.1 | -0.09±7.7 | -0.72 | 45 | 0.475 |
| 12/32wks | | | | | |
| **Within sub sum | 47.6±13.2 | 50.9±10.9 | -0.93 | 45 | 0.358 |
| **Albumin(g/L)** | | | | | |
| 12wks | 38.0±2.8 | 37.6±2.3 | 0.43 | 45 | 0.670 |
| 32wks | 39.2±1.9 | 39.1±2.0 | 0.18 | 45 | 0.857 |
| 12/32wks | | | | | |
| *Within sub diff | -1.3±3.3 | -1.5±2.7 | 0.25 | 45 | 0.804 |
| 12/32wks | | | | | |
| **Within sub sum | 77.2±3.5 | 76.7±3.4 | 0.42 | 45 | 0.674 |

*__Within sub diff__- The group mean of the individual participant measurement difference of the 12th and 32nd week

**__Within sub sum__- The group mean of the individual participant measurement sum of the 12th and 32nd week

## **Table.5** Distribution of Mean Serum Levels of Cholesterol, Urea, Creatinine and Random Blood Sugar

**Table 5 Distribution of mean serum levels of Cholesterol, Urea, Creatinine and Random blood sugar**

| | AB Grp (n=25) | BA Grp (n=22) | t | df | p-value |
|---|---|---|---|---|---|
| **Cholesterol(mmol/L)** | | | | | |
| 12wks | 5.5±1.5 | 5.8±1.5 | -0.6 | 44 | 50.524 |
| 32wks | 5.6±1.9 | 5.5±1.5 | 0.23 | 45 | 0.819 |
| 12/32wks | | | | | |
| *Within sub diff | -0.1±1.7 | 0.3±2.0 | -0.75 | 450.457 | |
| 12/32wks | | | | | |
| **Within sub sum | 11.0±3.0 | 11.2±2.3 | -0.21 | 450.836 | |
| **Urea(mmol/L)** | | | | | |
| 12wks | 5.7±3.0 | 6.1±2.6 | -0.42 | 450.676 | |
| 32wks | 4.9±1.3 | 5.1±1.7 | -0.30 | 45 | 0.763 |
| 12/32wks | | | | | |
| *Within sub diff | 0.8±2.7 | 1.1±1.7 | -0.33 | 450.744 | |
| 12/32wks | | | | | |
| **Within sub sum | 10.7±3.8 | 11.2±4.1 | -0.42 | 450.677 | |
| **Creatinine(umol/L)** | | | | | |
| 12wks | 87.7±30.1 | 77.4±21.2 | 1.35 | 450.185 | |
| 32wks | 92.3±27.3 | 80.1±19.7 | 1.75 | 45 | 0.088 |
| 12/32wks | | | | | |
| *Within sub diff | -4.6±6.9 | -2.7±9.2 | -0.81 | 45 | 0.421 |
| 12/32wks | | | | | |
| **Within sub sum | 180.0±57.1 | 157.4±39.9 | 1.56 | 450.127 | |
| **RBSugar(mmol/L)** | | | | | |
| 12wks | 5.7±2.4 | 5.5±2.3 | 0.323 | 450.748 | |
| 32wks | 5.6±1.4 | 5.4±1.3 | 0.37 | 45 | 0.712 |
| 12/32wks | | | | | |
| *Within sub diff | 0.2±2.1 | 0.1±1.4 | 0.1545 | 0.881 | |
| 12/32wks | | | | | |
| **Within sub sum | 11.3±3.4 | 10.9±3.5 | 0.37 | 450.713 | |

*__Within sub diff__- The group mean of the individual participant measurement difference of the 12$^{th}$ and 32$^{nd}$ week
**__Within sub sum__- The group mean of the individual participant measurement sum of the 12$^{th}$ and 32$^{nd}$ week

## **Fig.2** Laboratory Reference for Normal Values

| Nutritional Information | Average per tablet |
|---|---|
| Vitamin A | 5000 IU |
| Vitamin D3 | 800 IU |
| Vitamin E | 25 mg |
| Vitamin K | 90 µg |
| Vitamin C | 150 mg |
| Vitamin B1 (Thiamine) | 10 mg |
| Vitamin B2 (Riboflavin) | 7.5mg |
| Vitamin B6 | 3 mg |
| Folic Acid | 1500 µg |
| Vitamin B12 | 15 µg |
| Iron | 10 mg |
| Magnesium | 100 mg |
| Zinc | 15 mg |
| Iodine | 150 µg |
| Copper | 1.5 mg |
| Manganese | 4 mg |
| Selenium | 200 µg |
| Chromium | 75 µg |
| L-Cystine | 33 mg |
| L-Carnitine | 30 mg |
| Calcium pentothenate | 20 mg |
| Betacarotene(NaturalCarotenoids) | 50 mg |

| Metabolic Parameter | Normal Values |
|---|---|
| Serum GPT | <12U/L |
| Serum GOT | <12U/L |
| Serum Alkaline phosphatase | 9-35IU/L |
| Serum Cholesterol | 2.6-6.0mmol/L |
| Serum Urea | 2.6- 6.0mmol/L |
| Serum Creatinine | 44-133µmol/L |
| Serum Albumin | 38-42g/L |
| Random Blood Sugar | 3.3-8.3mmol/L |

Furthermore, in probable supportfor the result showing a lack of statistical significant effect on the metabolic parameters to the extent of the limitation of the power of this study, it was observed that in the first intervention period where the AB group received supplementation and the BA group did not receive supplementation, there was no statistically significant difference between the mean levels of the AB and BA groups for any of the metabolic parameters. Similarly, in the second intervention period where BA group now received supplementation and the AB group did not receive supplementation after a washout period, it was observed that there was no statistically significant difference between the mean levels of the BA and AB groups for any of the metabolic parameters.

The introduction and adherence to HAART for relatively long periods appeared to have influenced the nutritional states of the participants in this study as none of the participants at baseline had a BMI of less than 18kg/m$^2$. This is supported by some earlier studies that reported, that under nutrition which was a common state among HIV patients in the pre HAART era is now gradually shifting towards improved nutritional states in the post HAART era.[18,19] Further to this, Drain *et al*., also suggested that HAART initiation may improve some nutrient deficiencies seen in HIV patients and these observations may explain a lack of significant effect of micronutrient supplementation on the metabolic parameters in these patients who have been on HAART for relatively long periods.

It was generally observed at baseline, that more than 50% of the participants had normal serum levels of Cholesterol, Alkaline Phosphatase, Creatinine and Random blood sugar and more than 50% had high serum levels of Albumin, Urea, SGOT and SGPT. More specifically with respect to some of the metabolic parameters, Riddler *et al*. (2003) noted that HIV infection before treatment resulted in substantial decreases in serum cholesterol levels and upon HAART initiation was associated with increases in total cholesterol levels. Lucien *et al*. (2010) also reported that increases in SGOT levels were associated with SGPT levels upon treatment and treatment duration and furthermore, Alo *et al*. (2012) reported that high levels of serum creatinine and similarly high levels of serum urea were associated with the use of antiretroviral therapy.

All this further highlights the need for more studies on the metabolic parameters in HIV patients on long term HAART especially in resource limited regions where more people in these regions are now using and adhering to HAART for longer periods. In HIV patients using and adhering to long term HAART, the use micronutrient supplementation may be limited as these patients are now being associated with improved nutritional states and therefore

generally appear not to benefit from supplementation but rather proper and adequate dietary nutrition.

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