

## Derangement in Some Antioxidants among HIV-infected Persons in Calabar, Nigeria

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**Abstract:** Depletion of antioxidants is implicated in HIV infection but information on actual proportion of infected persons with the derangements remains vague. This study was conducted at University of Calabar Teaching Hospital Calabar, Nigeria. One hundred female (70%) and male (30%) HIV-infected adults (37.4±9.7 years) with 50 age and sex-matched control subjects participated. The CD<sub>4</sub>T-cell count, white blood cell (WBC) count, total protein (TP), albumin, globulin, zinc, selenium and vitamin C were analyzed by standard methods. Proportions of infected subjects with reduced WBC and CD<sub>4</sub>T-cell counts were 56% and 53% respectively. About a quarter (24%) of these subjects had low TP values, 44% had reduced albumin levels and 63% showed increased globulin values. Selenium deficiency occurred in 14%, zinc deficiency in 42% and vitamin C deficiency in 100% of the infected subjects. The CD<sub>4</sub>T-cell (496.33±209.87cells/μL) and WBC (4.65±1.52 x 10<sup>3</sup>/μL) of the infected persons were significantly lower compared to control subjects (788.54±294.71cells/μL, 5.54±1.28 x 10<sup>3</sup>/μL respectively). Among the infected persons, TP level (75.40±15.01g/L vs 70.86±8.03g/L) increased significantly, albumin level (34.04±8.44g/L vs 38.76±5.76g/L) was reduced, while globulin (41.42±15.85g/L vs 31.72±9.00g/L) showed a significant raise. There was raised selenium concentration (85.38±18.06μg/dL) but reduced levels for zinc (71.22±14.84μg/dL) and Vitamin C (0.37±0.09mg/dL) among the infected subjects compared to controls (56.26 ± 17.48μg/dL, 135.92 ± 22.75μg/dL and 1.12 ± 0.44mg/dL respectively). While different proportions of the infected persons showed deviations in the measured parameters, Vitamin C depletion was the commonest (100%) derangement among the studied population.

**Key Words:** Human Immunodeficiency Virus (HIV), Antioxidants, Derangement

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### I. Introduction

High prevalence of human immunodeficiency virus (HIV) infection and nutritional deficiencies are noted to be present in Africa where incidentally women of reproductive age are particularly vulnerable<sup>1</sup>. While it appears necessary to embark on widespread supplementation of implicated nutrients, certain concerns appear to hold back such a strategy. Pill-burden which is capable of limiting adherence among those already on antiretroviral therapy and cost implications especially in resource-poor settings are among some of the speculated limitations. Additionally, counterproductive developments such as observed increased transmission through breastmilk in association with vitamin A, the need for optimal dosing and issues of adverse effect have occasioned the consideration of other options such as integration of local diets<sup>2,3</sup>. To accommodate some of these concerns and establish a rationale for intervention, it may be necessary to have a cross-sectional view of the varying degrees at which common biomedical variables are deranged among those infected with HIV. Indeed, the subject of HIV infection and its terminal disease state; acquired immune deficiency syndrome (AIDS) continue to attract immense scientific studies with different perspectives to possible intervention options ranging from infection control in the general population to increasing life expectancy among those already infected. The quest to address the later has often led to investigating prognostic markers and strategies for delaying disease progression. As such most studies focus on detecting parameters prone to derangement as a result of the condition and the degree to which such variable deviation from normal. However, apart from comparison of values between infected and non-infected subjects, a yet informative approach would include determining actual proportions of the infected population with noted derangement. Such an approach could make academic findings more adoptable to intervention programmes.

Influencing intervention through academic research has not been without barriers especially in the area of clarity and purpose of information between researchers and policy makers. Apart from presenting important findings as mere data, there is also a need to use communication mode of conversations and stories that policy makers would appreciate<sup>4,5,6</sup>. Infection with HIV has been known to alter biomedical parameters to the extent that some of these variables now serve as markers of disease progression and predictors for survival<sup>7,8,9</sup>. While

outcome of the management of this infection may vary between persons and populations, information on the percentage of the infected population with actual derangements remains vague. This has rendered knowledge on the impact of the HIV scourge on specific populations incomplete. Moreover, studies on oxidative balance among infected persons have shown compromised status within this population; pointing to nutritional as well as immunologic challenges in association with the infection<sup>10,11</sup>. Adequate nutrition eventually extends to effective immunologic response which incidentally is the focus of the HIV onslaught. Thus, the approach of identifying prevalent deficiency states could explain the varying progress in managing the infection/ disease among different populations. Again, establishing the rate at which antioxidant depletion exists within populations of infected person has become a necessity in order to appreciate the magnitude of intervention that would be required.

## II. Materials and Methods

This study was carried out at the University of Calabar Teaching Hospital Calabar, Nigeria. The study subjects constituted 100 male and female HIV-infected adults with 50 age and sex-matched control subjects who were HIV sero-negative as at the time of this study. Ethical approval was obtained from the University of Calabar Teaching Hospital Medical Ethical Committee, while informed consent was given by each participant. Venous blood was collected aseptically by standard phlebotomy into appropriate sample containers for further analyses. Immunochromatographic method was employed for HIV screening The CD<sub>4</sub>T-cell count was conducted using Partecyflow cytometer, while white blood cell (WBC) count was carried out using Sysmex KX-21N from Sysmex Corporation, Japan. Zinc and Selenium (SEL) were assayed by Atomic Absorption Spectrophotometric (AAS) technique while vitamin C was done by Trichloroacetic acid Method. Total protein (TP) was estimated using Biuret Method and albumin (ALB) by Bromocresol Green method, while globulin was obtained by computation. Statistical analysis of data was carried out using SPSS 20.0. A two tailed P-value of ≤ 0.05 was considered indicative of a statistically significant difference.

## III. Results

The mean age of the adults who participated in this study was 37.4±9.7 years and more females (70%) than males (30%) were recorded. Marital status divided these participants into mainly single (49%) and married (44%) persons. A small proportion of 7% consisted of widows. The proportions of infected subjects with reduced WBC and CD<sub>4</sub>T-cell counts were 56% and 53% respectively. About a quarter (24%) of these subjects had low total protein values, 44% had reduced albumin levels and 63% showed increased globulin values. Only 14% of the infected persons were observed to be deficient while the rest had values within the reference range. Zinc deficiency was observed in 42% of the infected subjects while vitamin C deficiency occurred in all (100%) the infected subjects (Table 1).

The CD<sub>4</sub>T-cell (496.33 ± 209.87cells/μL) and WBC (4.65 ±1.52 x 10<sup>3</sup>/μL) of the infected persons were significantly lower compared to the control subjects (788.54 ± 294.71cells/μL, 5.54 ±1.28 x 10<sup>3</sup>/μL respectively). Among the infected persons, total protein level (75.40 ±15.01g/L vs 70.86 ±8.03g/L) increased significantly, albumin level (34.04 ± 8.44g/L vs 38.76 ± 5.76g/L) was reduced, while calculated globulin (41.42 ± 15.85g/L vs 31.72 ± 9.00g/L) showed a significant raise. There was raised selenium concentration (85.38 ± 18.06μg/dL) but reduced levels for zinc (71.22 ± 14.84μg/dL) and Vitamin C (0.37 ± 0.09mg/dL) among the infected subjects compared to the controls (56.26 ± 17.48μg/dL, 135.92 ± 22.75μg/dL and 1.12 ± 0.44mg/dL respectively) (Table 2).

**Table 1. Percentage distribution of HIV-infected subjects based on reduced, normal and elevated parameters.**

PARAMETERS				Reference range
	Reduced	Normal	Increased	
	%	%	%	
CD4 (cells/μL)	56	44	0	500-1,200 cells/μl
WBC (10 <sup>3</sup> /μL)	53	47	0	4.5-11.0x10 <sup>9</sup> /l
TP (g/l)	24	51	25	64-83g/L
ALB (g/l)	44	46	10	35-50g/l
Globulin (g/l)	6	31	63	2.0-3.5g/dL
SEL (μg/dl)	14	86	0	72-157μg/dl
ZINC (μg/dl)	42	58	0	70-120μg/dl
Vit. C (mg/dl)	100	0	0	0.6-2mg/dl

**Table 2:** Some haematologic and biochemical Parameters of HIV-infected patients compared with controls.

PARAMETERS	HIV-infected Patients n= 100	Controls n = 50	p-Value
CD4 (cells/ $\mu$ L)	496.33 $\pm$ 209.87	788.54 $\pm$ 294.71	0.000
WBC ( $10^3/\mu$ L)	4.65 $\pm$ 1.52	5.54 $\pm$ 1.28	0.001
TP (g/l)	75.40 $\pm$ 15.01	70.86 $\pm$ 8.03	0.047
ALB (g/l)	34.04 $\pm$ 8.44	38.76 $\pm$ 5.76	0.001
Globulin (g/l)	41.42 $\pm$ 15.85	31.72 $\pm$ 9.00	0.000
SEL ( $\mu$ g/dl)	85.38 $\pm$ 18.06	56.26 $\pm$ 17.48	0.000
ZINC ( $\mu$ g/dl)	71.22 $\pm$ 14.84	135.92 $\pm$ 22.75	0.000
Vit. C (mg/dl)	0.37 $\pm$ 0.09	1.12 $\pm$ 0.44	0.000

#### IV. Discussion

The participants of this study were mostly (70%) females of reproductive age (7.4 $\pm$ 9.7 years); highlighting the obvious vulnerability associated with this sub-population. More than half of the subjects had reduced WBC and CD<sub>4</sub>T-cell counts which suggests that majority of these infected persons could be immunosuppressed. Such individuals are thus more likely to succumb to the myriads of immune-related complications peculiar to HIV infection. The current observation that 44% of the infected persons had values within the reference range for CD<sub>4</sub>T-cell count is however a welcome development as an earlier survey in this population recorded a much lesser value of 5.3%<sup>12</sup>. Again more than half (63%) of the subjects recorded increased globulin; a consequence of the discordant total protein and albumin proportions. This also implies that most of the infected persons may be going through the compensatory mechanism that attends albumin depletion although only 44% recorded actual reduction in albumin level. In comparison with control subjects, total protein and globulin fraction were significantly (p<0.05) higher while albumin was significantly (p<0.05) lower among the infected persons. Albumin is considered the main extracellular molecule among plasma antioxidants that is responsible for plasma redox state. Its anti-oxidative ability has been ascribed to its multiple ligand binding capacities and free radical-trapping properties which are closely related to the structure and the redox state of the molecule. Free radical associated damage is interestingly considered an important factor in many pathological processes especially as it mediates protein modifications. Thus albumin represents both an abundant and important circulating antioxidant<sup>13,14</sup>. Its depletion in HIV infection has been observed in association with disease progression alongside a compensatory rise in the globulin fraction in order to ensure the maintenance of oncotic pressure<sup>8</sup>.

Selenium is considered important in inflammatory conditions due to the anti-oxidative function of selenoenzymes such as glutathione peroxidase and thioredoxin reductase in protecting cells from oxidative stress<sup>15</sup>. However, wide variations of selenium concentration are known to occur across human populations because its content in crops is dependent on soil levels and this differs geographically<sup>16</sup>. Serum selenium concentrations were generally high among the infected persons and majority of them had values within the reference range. Fourteen percent of the infected population however had selenium deficiency. Although often observed in reduced levels among HIV patients, it has been thought that selenium deficiency may also be more associated with some subsets of HIV population such as those with cardiomyopathy and opportunistic infections due to increased oxidative stress<sup>17,18</sup>. Since atherosclerosis which precedes ischemic heart disease results from accumulation of lipids and fibrous elements on arteries, the association between deficient serum selenium concentration and myocardial infarction reflects insufficiency in the inhibitory role of enzymatic antioxidants such as selenoenzyme glutathione peroxidase on lipoprotein oxidation<sup>19</sup>. Zinc is another antioxidant and is considered a molecular signal for immune cells. Its supplementation has been demonstrated to decrease plasma oxidative stress markers as well as generating of inflammatory cytokines<sup>20</sup>. Zinc deficiency was observed in 42% of the infected subjects and was significantly lower among them compared to the control group.

All the infected subjects were vitamin C deficient and the mean level was significantly reduced (p< 0.05) among the infected group. The observed 100% for vitamin C reduction among this HIV-infected population is quite informative. Whereas vitamin C has been considered essential for effective immune function through its influence on diverse cellular responses<sup>21</sup>, adequate consumption appears to be lacking. Consequently, its depletion is bound to occur especially within populations with obvious inflammatory challenges as seen in HIV infection. For a nutritional component that is readily available, the alarming percentage of infected persons suffering from its depletion is worrisome and worthy of immediate intervention. It is however important to note that owing to the observed sigmoidal relationship between oral dose and plasma/ tissue concentration, optimal

dosing is critical to intervention trials<sup>22</sup>. Exploring this possibility in addition to antiretroviral therapy may mediate better immune response among those infected.

## V. Conclusion

While different proportions of HIV-infected persons showed deviations in common antioxidants measured in this study, Vitamin C depletion was the commonest (100%) derangement among the studied population.

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