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ORIGINAL ARTICLE | DIETARY MICRONUTRIENTS AND HIV

Dietary Micronutrients and Gender, Body Mass Index and Viral Suppression Among HIV-Infected Patients in Kampala, Uganda

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ABSTRACT

Background: HIV/AIDS is a hallmark of immune suppression. Micronutrient deficiencies in diet and recurrent opportunistic infections play major roles in the lives of people living with HIV. Although benefits of providing adequate diet to HIV positive persons are well documented, the demand for key elements still remain unclear in particular settings, especially in low and middle-income countries.

Methods: This was a cross sectional analysis of baseline data collected from HIV-infected adults initiating antiretroviral therapy, and who were enrolled in a multivitamin supplementation trial. A food frequency questionnaire was used and intake were obtained as a product of quantities consumed. Adequacy was calculated as the proportion of Recommended Dietary Allowances (RDA). A chi square test and logistic regression analysis were used at p-value 0.05 to show significant associations.

Results: Mean intakes were above minimum requirements for analyzed micronutrients with the exception of Calcium and Iron. Participants who met RDA intakes were as follows: highest (≥ 80%) for Magnesium, Selenium, Zinc and Vitamins B2, B6, B9, C and E; moderate (50% to <80%) for Vitamins B3, and A; and lowest (≤50%) for Iron (30%), Calcium (14.9%), Vitamins B12 and B1. Gender differences in met RDA were observed for Iron, Selenium, Zinc, Vitamins A, B1, B3 and E. In multivariable analyses, nutritional status and CD4 count had no influence on meeting RDA for majority of micronutrients such as magnesium, Selenium, B class vitamins (B1, B2, B3, B6, B9, B12), vitamin (A, C, and E), Zinc and Calcium, but not including iron.

Conclusion and Global Health Implications: Diets consumed by the study participants were low in most protective nutrients (Iron, Calcium, Zinc, Vitamin A, B1, B3, and B12). This deficiency was more common among females than males, and irrespective of BMI or CD 4 count. Findings warrant further investigation on the impact and cost implications for suplementation interventions that target the elements lacking in the diets of people living with HIV in similar low-resourced settings.

Key words: • Recommended Dietary Allowances • Micronutrients • Dietary intakes • Body Mass Index • CD4 cell count • HIV/AIDS • Uganda

1. Introduction

The HIV/AIDS epidemic continue to burden populations where malnutrition is also highly prevalent.[1] This effect is mostly experienced in Sub-Saharan African countries, a region that contributes 68% to the global prevalence for people living with HIV (PLHIV).[2,3] Whereas Uganda's population is challenged by food insecurity, we note a compromise on the nutritional status of PLHIV. This often may lead to a faster progress to AIDS among malnourished persons as a result of the fuelling effect of opportunistic infections. In Kampala area, a survey done in 2013 showed high levels of micronutrient deficiencies in the general population as follows: 98% for calcium; 75% for Iron; and 69% for vitamin A.[4] The fact that HIV/AIDS triggers biological and social factors that impact the individual's ability to acquire, ingest and absorb micronutrients warrants further studies. Moreover, deficiencies of vitamins A, E, B6, B12 and C, carotenoids and Selenium are common among HIV-infected populations.[5]

1.1. Background of the Study

Micronutrients play important functional roles in the human immune response,[6-8] and quality of diets is a major determinants of HIV disease severity and mortality in ART-naïve PLHIV.[9] The fact that micronutrients can have negative effects on HIV disease progression if consumed inappropriately,[10-13] warrant further studies in order to help in designing suitable interventions.[14,15] A number of studies conducted among HIV-infected adults during the pre- highly active antiretroviral therapy (HAART) era, have shown that multivitamin supplementation enhances immune reconstitution, reduces viral load, improves overall clinical outcomes, and reduces mortality.[16-18] However, the extent of meeting the daily requirements and its correlation with gender and physiological state of HIV-positive patients initiating HAART in Uganda remain unknown. The trial for multivitamin supplementation whose baseline data is analyzed in this paper was conducted between 2010 and 2013; the study was among HIV-positive adults initiating antiretroviral therapy at the Infectious Diseases Institute in Kampala Uganda.[19] The objectives of the study were to: (1) determine the proportion of HIV seropositive patients consuming diets that meet the Recommended Daily Allowances (RDA) of selected micronutrients; (2) assess the association of micronutrient intakes with BMI among HIV positive patients initiating HAART; and (3) assess the association of micronutrient intakes with CD4 cell count among HIV-positive patients initiating HAART.

2. Methods

A detailed description of the methods used in the parent micronutrient trial has been previously described.[19] This article describes the relevant details of methods used to derive data used in the analysis of results.

2.1. Setting and Participants in the Parent Trial

The parent study was conducted between April 2010 and December 2013 at the Infectious Diseases Institute (IDI), Makerere University College of Health Sciences, in Kampala Uganda. A total of 400 HIV-positive adults initiating ART were enrolled into the trial. Patients were eligible for enrolment into the trial if they were: (a) aged at least 18 years, (b) confirmed HIV-positive, (c) initiating anti-retroviral therapy at the time of enrolment or had been on HAART for no longer than 6 months, (d) had no intention of migrating, or re-locating more than 20 km outside of the IDI within the next 18 months following enrolment, (e) agreed to allow home visit(s) and subsequent follow-up contacts as part of the study, and (f) provided written informed consent. Women with a positive pregnancy and individuals who were very ill and unable to consent were excluded from participating in the trial. This is because, iron and folic acid supplementation, being a part of the standard of care for pregnant women per Uganda Ministry of Health Standard, would influence modification of trial outcomes and yet the study would lack sufficient statistical power to examine this factor.

2.2. Study Design

Results presented in this article are based on analysis of baseline data collected from HIV positive adults participating in a trial of multivitamin supplementation. We used data from all trial

participants since the sample size was already estimated/calculated and documented elsewhere.[18] During the trial period, assessment data were collected at baseline, at 3 months and subsequently at 6 months. For this study, we only used baseline data as we would not have enough statistical power to examine micronutrient supplementation as an effect modifier on health status parameters. Clinically, participants were given a full clinical examination and laboratory parameters including assessments of complete blood counts (CBC), CD4 counts, and anthropometric measurements. Anthropometry and dietary information including, weight and mid-upper arm circumference (MUAC), information on dietary intakes was collected at baseline, month 3 and subsequently six monthly to assess nutritional status of study participants.

2.3. Measurements

At baseline, a detailed background information questionnaire was administered to trial participants to obtain socio-demographic data, age, parity, education, residence, employment status, socio-economic status variables, marital status, and past/current use of tobacco, alcohol and other substances, etc. Anthropometric measurements including weight, height and mid upper arm circumference (MUAC) were measured to determine nutritional status. Instruments were calibrated at regular intervals and trained study nurses performed anthropometry measurements using the standard techniques. Based on the experience gained from the completed trials of nutrition and infection in Tanzania in a similar HIV-infected population, this study adapted and validated questionnaires, (7-day food frequency questionnaire (FFQ) and 24-hour recalls) from the Tanzanian population. The FFQ was developed based on an extensively used version in Tanzania which has been recently validated.[20] Given the similarity in food habits in Uganda, we adopted the questionnaire but revised the list of foods to be sure it includes foods not included.

The FFQ that included a 24-hour and 7-day diet recalls was administered in combination. The FFQ comprised of an 87-item food recipe list, and each participant was asked to report the frequency and amount of their typical consumption of each food item over the specific recall period. In order to standardize the food quantities consumed, we used the common household utensils in Uganda as the portion sizes, to help participants estimate quantities of foods consumed. If a participant reported to have eaten any food item recipe listed during the recall period, they were asked to indicate the consumed portions. In a separate exercise, each of the food recipe portion size was weighed, and data on weight (in grams) of each portion size for each food recipe listed on the FFQ was stored in a database for use during analysis. The study employed skilled data collectors and research supervisors. While collecting data, trained research assistants who were closely supervised, used the household utensils for illustration to determine portions of food intakes for a particular individual during the data collection process. On a daily basis, the supervisors would check through the collected data for errors and completeness to ensure high quality data.

2.4. Study Variables

The dependent variable investigated in this study was intake of diets that meet the Recommended Daily Allowances (RDA) for each micronutrient. The independent variables included sex, BMI and CD4 cell count status of the study participants. The covariates considered in the study included participants' duration on HAART and use of multivitamin.

2.5. Statistical Analysis

During data cleaning, individual daily requirements by age and sex-specific energy-only cut-off point were used, as a recommended measure to exclude over/under estimated nutrient contents.[21-23] By this assumption, we excluded individuals with intakes below the Basal Metabolic Rates (BMR) requirement for adults (1231 kcal for females and 1444 kcal for male). Also, very high intakes (2 or 3 times the interquartile range) were treated as outliers and were excluded from the analysis.

The first step during analysis was to obtain the weight of each food reported to have been consumed by the participant during the 24-hour recall period. This was obtained as the product of number of

portion sizes consumed, and the weight of each portion size. To estimate the quantity of the various micronutrients consumed by the participants, we used the Tanzania Food Composition Tables (TFCT) to estimate the micronutrient contained in the weight consumed.[24-25] The TFCT are based on the World Food Dietary Assessment System (WFDAS) which include the International food composition tables developed as part of the world food dietary assessment program to provide values for the amount of nutrients that a food item contains.[26-28] The TFCT tables provide all micronutrient values with adjustments for moisture and waste, and nutrient content of each food is expressed per 100 gram (g) edible portion. The TFCT provide estimates of the various foods commonly consumed in Tanzania, which are largely similar to foods commonly consumed within the East African Region. In the analysis, micronutrient food values of food items not found in the TFCT, were imported from the United States department for agriculture (USDA) national nutrient database.[29]

The micronutrient intake over the 24-hour reference period for each food was calculated as the product of the weight of the food consumed and the respective micronutrient weight in the TFCT, divided by the unit weight used in the TFCT. To obtain the total intake for each type of nutrient consumed, summation of nutrient content in all food items consumed by the participant over the 24-hour reference period was obtained.

Finally, the percentage of the Recommended Dietary Allowances (RDA) for each micronutrient consumed by each participant was obtained[24,26] and a participant was classified as having met the (RDA) for each micronutrient or not. A value of at least 100% was treated as adequate intake, whereas a value less than 100% was inadequate intake. Thus, we report mean micronutrient intake values and their respective standard deviations (SD), as well as the percentage of participants meeting RDAs for each micronutrient. To show significant associations, a chi square test and logistic regression analysis were used (at p value 0.05) at bivariate and multivariable levels. On analysing data, duration on HAART and use of multivitamins were treated as confounders. In multivariable analyses only significant outcome variables at bivariable analysis were considered. In the findings, only significant variables at multivariable analysis were presented. Because of the importance on immune reconstitution and previously reported deficiencies among PLHIV elsewhere,[5] analysis was focused on the following micronutrients: Calcium, Iron, Magnesium,, Selenium, Zinc, and Vitamins A, B1,B2, B3, B6, B9, B12, C and E.

2.6. Ethical Approval

The trial protocol in which this study was nested was approved by the Scientific Review Committee of the infectious Diseases Institute at Makerere University College of Health Sciences, the Institutional Review Board of Harvard School of Public Health and that of Makerere University School of Public Health. Permission was obtained from the District Health office, sub-county chiefs, and local council leaders. The investigator provided explanation of the purpose, risks and benefits of the study to the community members before soliciting for their participation in the study. Individuals were also given assurance that the information they provided was to be treated with confidentiality. They were informed of their right to withdraw from the study at any time without fear of any negative repercussions. Participants were requested to give their verbal consent.

3. Results

3.1. Participant Characteristics

A total of 400 HIV infected patients were enrolled in the parent trial, of which 227 (69%) were female, 290 (72%) were older than 30 years with an overall average of 35.8 years (SD= 9.0). Only 88 participants (22%) reported using multivitamins prior to enrolment into the trial for a median duration of one month, and 200 (50%) had been initiated on HAART within the past six months for a median duration of 1.9 months (Interquartile range = 0.5–3.9). More details about baseline characteristics of participants is reported elsewhere[29]. Following a data cleaning process, to reduce reporting bias, 368 participants were considered for analysis. 51(13.86%) had no income generating activities, 221(60.5%) had informal employment, 11(3.44%) had semi-skilled

employment, 72(19.55%) had skilled employment. 12 (3.26%) had no formal education, 138 (37.5% did not complete primary level, 51(13.86%) completed primary education, 75(20.38%) did not complete o-level, 37(10.05%) completed o-level, 3(0.82%) did not complete A-level, 14(3.8%) completed A-level, 37(10.06%) attended tertiary education. 94(25.54%) were married, those staying with sexual partners were 30(8.15%), 32(8.7%) single, 63(17.12%) were widowed, 1(0.27%) was divorced and 110 (29.89%) separated with their spouses. 279(75.82%) of respondents had a CD 4 count <200, 75(20.38%) had a CD 4 count between (200-349), and 14(3.8%) had a CD4 count ≥350. Majority had a normal BMI (240, 65.22%), followed by those who were overweight (98, 26.63%) and 30(8.15%) were thin.

3.2. Overall Intakes from Diets as a Source of Micronutrients

Overall, mean intakes for Selenium, magnesium, Zinc, and for Vitamin A, B1, B2, B3, B6, B9, B12, C, and E were above the minimum daily nutrient requirements except Calcium, and Iron.

From the foods reported to have been consumed by participants in the past 24 hours, highest proportions (≥80%) of participants who met RDA intakes were observed for the following micronutrients: Magnesium (95.1%); Selenium (90.2%); Zinc (83.1%); Vitamin B2 (98.1%); Vitamin B6 (89.7%); Vitamin B9 (90.5%); and Vitamin C (99.5%). However, moderate proportions (50% to <80%) of participants consumed adequate intakes of Vitamin B3 (75.5%) and Vitamin A (53.0%). Lowest proportions (≤50%) of participants consuming adequate intakes were observed for Iron (30%), Calcium (14.9%), Vitamin B1 (47.0%), and B12 (30.2%).

3.3. Micronutrient Intakes by Gender

Study findings indicated a significant difference in met RDA at p value ≤ 0.05; 95% CI, between males and females for Iron 65% Vs 14%; Selenium 95.5% Vs 87.9%; Vitamin B1 99% Vs 24.8%; Vitamin B3 67.3% Vs 80.0%; and Vitamin A 42.7% Vs 57.4%, respectively (Table 1). Small differences were observed for Zinc (82.7% Vs 83.3%) and Vitamin E (80.9% Vs 81.8%). Comparisons showed that males had a higher proportion in met RDA intakes for majority of nutrients (Iron, Selenium, Vitamin B1) except for Vitamin A and B3. We also noted a very small difference for Zinc and Vitamin E.

3.4. Micronutrient Intakes by Body Mass Index (BMI)

Majority of participants 240 (65.2%) had a normal weight, followed by overweight 98 (26.6%) and the lowest proportion as being underweight 30 (8.2%). Irrespective of nutritional status, the lowest proportion of respondents, across the three weight levels, with inadequate intakes were reported for magnesium (6.67%, 5.42%, 3.06%), Vitamin B2 (3.33%, 3.33%, 4.08%), Vitamin B6 (3.33%, 11.67%, 9.18%) Vitamin B9 (10.0%, 10.42%, 7.14%), Vitamin C (3.33%, 0.42%, 0.00%), Vitamin B3 (26.67%, 26.25%, 19.39%), vitamin E (20.0%, 17.08%, 21.43%) with a significant difference was observed for selenium (10.00%, 9.58%, 10.20%; at p=0.030). A significant proportion of respondents had unmet RDA irrespective of nutritional status for: calcium (73.33%, 86.25%, 85.71%), Vitamin A (43.33%, 50.00%, 4 0.82%), B12 (46.67%, 29.17%, 27.55%), B1 (63.33%, 48.75%, 60.20%), and a significant difference was noted among individuals by nutritional status class for Iron (66.67%, 65.42%, 83.67%: p=0.002). Having adjusted for duration on HAART and use of multivitamins, overweight patients were almost three times more likely to have unmet RDA for Iron (OR= 2.54, CI (1.00-6.44, p=0.005) (Tables 2 and 3).

3.5. Micronutrient Intakes by CD4 Cell Counts

Majority (279, 75.82%) of patient initiating HAART had a low CD4 cell count >200, followed by CD4 cell count between 200-349.99 (75, 20.38%) and least (14, 3.8%) among CD4 cell count ≥350. Irrespective of CD4 count, the lowest proportion with inadequate intakes were reported for magnesium (5.02%, 2.67%, 14.29%), Selenium (10.04%, 6.67%, 21.43%), zinc (16.25%, 13.33%, 35.71%), Vitamin B2(2.51%, 0.00%, 0.00%), vitamin B9(10.00%, 10.42%, 7.14%), B6 (9.68%, 12.00%, 14.29%), Vitamin B3 (23.66%, 26.67%, 28.57%), Vitamin E (17.2%, 21.33%, 28.57%), vitamin B12 (32.26%, 25.33%, 14.29%). A considerable proportion of respondents had inadequate diets for

Table 1: Adequacy of micronutrient intake among HIV seropositive patients by sex specific RDA

Micronutrient	Sex	RDA	Mean 24hr intake (+SD)	%meeting RDA	P-value
Calcium(mg)	Male	1000	600 (474.7)	17.2	0.414
	Female	1000	588 (511.7)	13.9	
	Both sexes		592 (500.3)	14.9	
Iron(mg)	Male	23	32 (17.4)	65.0	0.000
	Female	48	29.8 (17.8)	14.0	
	Both sexes		30.4 (17.7)	30.0	
Magnesium(mg)	Male	260	860 (467.3)	95.4	0.588
	Female	220	745 (441.3)	95.0	
	Both sexes		779.9 (451.6)	95.1	
Niacin(mg)	Male	19.8	31 (20.2)	67.3	0.016
	Female	14.5	28.5 (19.1)	80.0	
	Both sexes		29 (19.5)	75.5	
Selenium(µg)	Male	26	169 (120.1)	95.5	0.027
	Female	34	162 (128.9)	87.9	
	Both sexes		164 (126.3)	90.2	
Zinc(mg)	Male	11	25 (14.8)	82.7	0.020
	Female	8	23 (14.5)	83.3	
	Both sexes		23.3 (14.6)	83.1	
Vitamin A(mg)	Male	600	850 (1359.7)	42.7	0.010
	Female	500	897 (981.1)	57.4	
	Both sexes		883 (1106.2)	53.0	
Vitamin B1(mg)	Male	1.2	45 (93.8)	99.0	0.000
	Female	0.9	65 (158.5)	24.8	
	Both sexes		59 (142.5)	47.0	
Vitamin B2(mg)	Male	2.4	44 (40.9)	99.1	0.679
	Female	2.4	40 (44.2)	97.7	
	Both sexes		41 (43.3)	98.1	
Vitamin B6(mg)	Male	1.5	4.9 (3.1)	92.7	0.263
	Female	1.5	4.3 (3.4)	88.4	
	Both sexes		4.5 (3.3)	89.7	
Vitamin B9(µg)	Male	200	610 (408.2)	90.0	0.835
	Female	170	583 (457.2)	90.7	
	Both sexes		591 (442.7)	90.5	
Vitamin B12(µg)	Male	2.4	4 (8.4)	32.7	0.247
	Female	2.4	3.8 (8.2)	29.1	
	Both sexes		3.9 (8.3)	30.2	
Vitamin C(mg)	Male	30	583 (515.2)	98.2	0.652
	Female	30	528 (582.8)	100.0	
	Both sexes		544 (563.3)	99.5	
Vitamin E(mg)	Male	14	72 (59.2)	80.9	0.048
	Female	14	75 (66.3)	81.8	
	Both sexes		74(64.2)	81.5	

Table 2: Bivariate analysis for micronutrient intake by BMI among HIV+ patients initiating HAART

Micronutrient	BMI	HIV+ adults (unmet RDA by row%)	OR	CI	Chi square test (P value)
calcium	≤18.4	73.33			
	18.5-24.99	86.25	2.28	0.94-5.55	0.217
	>25	85.71	2.18	0.81-5.86	
Iron	≤18.4	66.67			
	18.5-24.99	65.42	1.00	0.42-2.11	0.002
	>25	83.67	2.56	1.01-6.49	
Magnesium	≤18.4	6.67			
	18.5-24.99	5.42	0.80	0.17-3.74	0.568
	>25	3.06	0.44	0.07-2.77	
Niacin	≤18.4	26.67			
	18.5-24.99	26.25	0.97	0.41-2.31	0.382
	>25	19.39	0.66	0.25-1.71	
Selenium	≤18.4	10.00			
	18.5-24.99	9.58	0.95	0.26-3.38	0.03
	>25	10.20	1.02	0.26-3.98	
Zinc	≤18.4	16.67			
	18.5-24.99	18.33	1.12	0.40-3.09	0.515
	>25	13.27	0.76	0.24-2.35	
Vitamin A	≤18.4	43.33			
	18.5-24.99	50.00	1.31	0.60-2.81	0.280
	>25	40.82	0.90	0.39-2.06	
Vitamin B1	≤18.4	63.33			
	18.5-24.99	48.75	0.55	0.25-1.20	0.077
	>25	60.20	0.87	0.37-2.04	
Vitamin B2	≤18.4	3.33			
	18.5-24.99	3.33	1.0	0.12-8.28	0.944
	>25	4.08	1.2	0.13-11.48	
Vitamin B6	≤18.4	3.33			
	18.5-24.99	11.67	3.8	0.50-29.2	0.260
	>25	9.18	2.9	0.35-24.14	
Vitamin B9	≤18.4	10.00			
	18.5-24.99	10.42	1.04	0.29-3.69	0.630
	>25	7.14	0.69	0.16-2.86	
Vitamin C	≤18.4	3.33			
	18.5-24.99	0.42	0.12	0.01-1.99	0.1703
	>25	0.00	-	-	-
Vitamin B12	≤18.4	46.67			
	18.5-24.99	29.17	1.04	0.29-3.69	0.6301
	>25	27.55	0.69	0.16-2.86	
Vitamin E	≤18.4	20.00			
	18.5-24.99	17.08	1.21	0.46-3.15	0.6356
	>25	21.43	0.91	0.33-2.53	

Table 3: Multivariate analysis for association of micronutrient intake by BMI among HIV+ patients initiating HAART after adjusting for duration on HAART and use of multivitamins

Micronutrient	BMI	Adjusted OR	CI	Chi square test (P value)
Iron				
	≤18.4			
	18.5-24.99	0.92	0.41-2.06	0.045
	>25	2.59	1.02-6.591	

Table shows only significant findings

calcium (84.33%, 85.33%, 100.0%), Vitamin A (48.39%, 44.00%, 35.71%), B1 (51.97%, 52.00%, 78.57%) and a significant difference by CD4 category was noted among individuals by CD4 for Iron (67.03%, 80.00%, 85.71%; P=0.032); (significant level p=0.05). Having adjusted for duration on HAART and use of multivitamins, participants with higher CD 4 counts (200-349.99 and >350) were more likely to have unmet RDA for Iron (OR= 2.02, 3.02; CI (108-3.79, 0.65-14.02) p=0.035) (Tables 4 and 5).

4. Discussion

This study evaluated dietary intakes as a source of essential micronutrients among HIV infected adults initiating HAART. The findings indicated that over 90% of respondents had met RDA intakes for Magnesium, Selenium, B class vitamins (B2, B6, B9), Vitamin C and E. However, we note that a significant proportion of respondents had unmet RDA for important elements such as; Vitamin A, B class vitamins (B1, B3 and B12), iron, zinc, calcium, among which deficiencies differed by gender. Unmet RDA for Iron was highest among overweight patients.

Several studies have shown that minerals/trace elements are key in maintaining health, and reducing mortality despite the stage of immunodeficiency virus infection. For instance, Vitamin C has been found to affect immune function in several ways; It can stimulate the production of interferons; one of the protein that protects cells against viral attack[30]. Observational studies have so far indicated very good anti-oxidant properties of Selenium and supplementation programs using this nutrient have led to improvements in recovery of symptomatic patients[31,32]; B complex vitamins (B1, B2, B6, B9, B12) have proven to be key elements in maintaining well-being of person infected with HIV, and supplementation studies have shown delays in progress of HIV to AIDs[11,33,34]. Similarly supplementation with large doses of vitamin C and E led to a reduction in viral load[16].

While micronutrient are important blockers to HIV progression, deficiencies are known to occur among HIV patients irrespective of the stage of disease progression. The situation is even made worse among HAART naïve patients. In HIV care for asymptomatic persons, dietary supplementation with vitamin A,B, and C is recommended and should be given in once a day dose to all patient. Deficiencies observed in this study are consistent with findings reported by Oyango et al among HIV positive adults attending a sub-hospital in kenya[17]. This similarity may be explained by the quite similar foods known to be grown, and availed in the East African market, which in turn are commonly consumed by majority of the east African population. It is therefore important to note, the considerably low consumption of minerals/elements present in diets of HIV patients.

Our findings further indicated that deficiencies for most nutrients were common among females compared to males. The study noted high proportions in unmet RDA for Iron, Selenium, and Vitamin B1 among females, whilst Niacin and Vitamin A were high among males. Studies have indicated lower nutrient intakes for Zinc, Calcium and Iron among women than males and this may be attributed to consumption of low intakes which are deficient of nutrients.[36,37] On the other hand, Uganda's household diet is predominantly vegetable and tubers.[4,37] The fact that males have a higher chance of consuming foods away from home, may increase chances of consuming a variety of foods than women who mostly depend on home prepared meals.

Table 4: Bivariate analysis for micronutrient intake by CD4 cell count among HIV+ patients initiating HAART

Micronutrient	CD 4 cell count	HIV+ adults (unmet RDA by row %)	OR	CI	Chi square test (P value)
Calcium					
	>200	84.23			
	200-349.99	85.33	1.08	0.53-2.23	0.813
	≥350	100.00	1.00	-	-
Iron					
	>200	67.03			
	200-349.99	80.00	1.97	1.0-3.6	0.032
	≥350	85.71	2.95	0.65-13.5	
Magnesium					
	>200	5.02			
	200-349.99	2.67	0.52	0.11-2.33	0.253
	≥350	14.29	3.15	0.64-15.47	
Niacin					
	>200	23.66			
	200-349.99	26.67	1.17	0.65-2.09	0.812
	≥350	28.57	1.29	0.39-4.25	
Selenium					
	>200	10.04			
	200-349.99	6.67	0.64	0.23-1.72	0.272
	≥350	21.43	2.44	0.64-9.29	
Zinc					
	>200	16.85			
	200-349.99	13.33	0.76	0.36-1.58	0.166
	≥350	35.71	2.74	0.87-8.55	
Vitamin A					
	>200	48.39			
	200-349.99	44.00	0.83	0.50-1.39	0.544
	≥350	35.71	0.59	0.19-1.81	
Vitamin B1					
	>200	51.97			
	200-349.99	52.00	1.00	0.60-1.67	0.128
	≥350	78.57	3.38	0.92-12.41	
Vitamin B2					
	>200	4.30			
	200-349.99	1.33	0.30	0.038-2.35	0.177
	≥350	0.00	1.00	-	
Vitamin B6					
	>200	9.68			
	200-349.99	12.00	1.27	0.57-2.83	0.755
	≥350	14.29	1.55	0.33-7.32	

(*Contd...*)

Table 4: (*Continued*)

Micronutrient	CD 4 cell count	HIV+ adults (unmet RDA by row %)	OR	CI	Chi square test (P value)
Vitamin B9					
	>200	9.68			
	200-349.99	8.00	0.811	0.32-2.04	0.761
	≥350	14.29	1.555	0.33-7.32	
Vitamin B12					
	>200	32.26			
	200-349.99	25.33	1.40	0.78-2.50	0.186
	≥350	14.29	2.86	0.62-13.03	
Vitamin C					
	>200	0.72			
	200-349.99	0.00	-	-	-
	≥350	0.00	-	-	
Vitamin E					
	>200	17.2			
	200-349.99	21.33	1.31	0.69-2.46	0.463
	≥350	28.57	1.92	0.58-6.39	

Table 5: Multivariate analysis for association of micronutrient intake by CD 4 cell count among HIV+ patients initiating HAART after adjusting for duration on HAART and use of multivitamins

Micronutrient	CD 4 cell count	Adjusted OR	CI	Chi square test (P value)
Iron				
	>200			
	200-349.99	2.02	1.08-3.79	0.035
	≥350	3.02	0.65-14.02	

Table shows only significant findings

Findings indicated no difference in meeting the RDA for most micro nutrients by individual's nutritional status, except for iron. Similar findings were observed by Sirotin et al.[38] This affirms that, prior to implementing a supplementation program, undertaking a primary investigations will help improve the effect of positive outcome by targeting population related dietary deficiencies. Similarly, nutritional status may not be a good indicator for accessing eligibility for nutrient supplementary interventions among PLHIV.

The study also observed no significant association in individual diets and CD4 cell count for majority of micronutrients, except iron. This is in support of studies which showed a common occurrence of micronutrient deficiencies in HIV infection, and occur at all stages of immune deficiency, including asymptomatic stage.[2,3,4] This affirms that diets of HIV+ adults initiating HAART are likely to lead to an equal exposure to immune suppression irrespective of CD4 cell count. Eventually, the consequence will be accelerated progression from HIV to AIDS.

4.1. Study Limitation

The 24-hour dietary recall used in the study can be over/underestimated based on the individual daily intakes. On the other hand, misreporting of the actual intakes among the study participants was expected as a result of recall bias. To cater for these limitations, we used a combination of 24 hour and 7-day dietary assessment to adjust for estimates of association between RDA, and individual health outcomes (BMI,

and CD4). Likewise, the study employed skilled data collectors with a knowledge background in nutrition. These were further trained on using illustrations/ aiding objects to assist participants in reporting correctly. The study further employed a screening process for misreporting at data cleaning level to identify and exclude outliers based on age and sex specific energy intake cut-offs as indicated in the analysis section. The study methodology led to enrolment of HIV positive patients coming to the facility for care and did not consider HIV patients who remain in the community and the in-infected persons as a control group. The deficiencies in diets may be prevalent in the community and this may lead to low external validity that warrant further study.

5. Conclusion and Global Health Implications

These findings will help to inform the design of nutrition supplementation interventions for Uganda and other similar settings that target HIV positive patients. They help to reveal the deficiencies of key vitamins and minerals in diets of PLHIV. Providing supplements to individuals with diets whose deficiencies is known may produce bigger impact at less costs in care. These findings warrant further investigation on the impact and cost-effectiveness of interventions that target supplying the lacking micronutrients and minerals in diet of PLHIV in similar settings.

Complaince With Ethical Standards

Conflicts of Interest: *The authors declare that they have no competing interests.* ***Financial Disclosure:*** *The authors declare that they have no financial interests.* ***Funding/support:*** *Research findings reported in this article were supported by the Eunice Kennedy Shriver National Institute of Child Health & Human Development of the National Institutes of Health [grant number R01HD060333]. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.* ***Ethics Approval:*** *The trial protocol in which this study was nested was approved by the Scientific Review Committee of the Infectious Diseases Institute at Makerere University College of Health Sciences, the Institutional Review Boards of Harvard School of Public Health and that of Makerere University School of Public Health. It was registered under clinical trials: NCT01228578.* ***Acknowledgements:*** *We acknowledge the trial staff including, Irene Nakatudde, Joanita Murungi, Paul Gonza, Rita Kisenyi, Aidah Zawedde, Eva Laker and Esther Lubwama. We also acknowledge the input by Barbara Castelnuovo, Fred Wabwire-Mangen, Donna Spiegelman and Emily Rose Smith. We are grateful to the trial participants, the support by all IDI staff; and the trial DSMB members Drs. David Schoenfield, Donald Thea, Tom Lutalo and Hanifa Bachou.*

Key Messages

- A considerable proportion of HIV infected adults initiating HAART consume diets deficient of Iron, Calcium, Zinc, Vitamins A, B1, B3, and B12.
- Dietary deficiencies differed by gender and are more prevalent among females.
- Nutritional status and CD4 cell count have no effect on the observed deficiencies in diets of HIV-infected adults who are initiating Highly active antiretroviral therapy (HAART).
- Supplementation programs that target known deficiencies in diets may produce bigger impact at less costs in care.

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