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RESEARCH ARTICLE

Clinical Assessment of Nutritional and Metabolic Status in HIV Outpatients

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Abstract:

Background:

After the World Health Organization's first technical consultation on Nutrient Requirements for People Living with HIV/AIDS in Geneva, 2003, a lot of research questions that are considered crucial for enhancing our understanding of the interaction of nutrition and HIV infection were raised and until this moment, left unanswered. To gain a better understanding of HIV and nutrition, we implemented a comprehensive approach. The aim of our study was to assess the nutritional and metabolic status in order to enhance the provision of medical care to people living with HIV.

Methods:

45 HIV patients and 32 healthy volunteers were enrolled in the study. Within the HIV group, 32 (71%) were male and 13 (29%) female. Only 7 (15%) were ART naïve. Overall their median age, CD4 count and viral load were 30 years (IQR: 28-40), 407 (IQR: 357-490) cells/mm³ and 500 (IQR: 0-1000) copies/ml, respectively. None of the participants in the HIV group had any active infection. Food intake by monthly dietary recall was determined. Body composition was measured using bioelectrical impedance analysis. The selected biochemical parameters were evaluated and the resting metabolic rates were calculated using indirect calorimetry to accurately understand the metabolism of participants.

Results:

Participants in the HIV group did not meet the recommended daily allowance level (RDA) of carbohydrate requirements. The fat-free mass significantly decreased in the HIV group ($P < 0.05$). Resting energy expenditure was excessive in the HIV group compared to the control group ($P < 0.05$). Values of urea nitrogen concentration, fat and protein oxidation rates in the HIV group significantly increased ($P < 0.01$). The carbohydrate oxidation in the HIV group significantly decreased ($P < 0.01$).

Conclusions:

The study reveals a catabolic status in the HIV group and suggests an adjustment in the nutrient RDA to compensate such status. Further investigation should be extended to vulnerable population group particularly children.

Keywords: Bioelectrical impedance, HIV infection, Indirect calorimetry, Metabolism, Nutritional status, Resting energy expenditure.

Article History

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1. INTRODUCTION

The global burden of HIV is approximately 33 million, with 67% of those affected living in impoverished sub-Saharan Africa, where malnutrition is rampant because the daily household income is less than 1 US dollar per day. Nevertheless, food security in HIV patients is a problem for developing and developed countries. Immunodeficiency and malnutrition lead to a decrease in body weight and “waste

syndrome,” which is defined as the loss of body weight by 10% or more. Despite the introduction of antiretroviral therapy (ART), weight loss remains one of the leading AIDS-defining clinical conditions [1 - 3]. Studies have shown a high percentage of weight loss (11 out of every 100 patients per year) among outpatients receiving ART [4]. A cohort study revealed 33.6% cases of weight loss in patients with HIV infection, even though 45% of those observed had a CD4 count of more than 350 cells / mm³ [5]. The initial report revealed that HIV individuals with weight loss had an initial viral load of less than 400 cells / mm³ [6, 7]. These data suggest that weight loss is not solely related to viral load, and the scale of

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weight loss in PLWH remains significant despite ART intervention. Morbidity and mortality associated with eating disorders and the need for a multidisciplinary approach are well reported in the literature [8]. Studies revealed that the death of HIV- patients occurred when their weight fell below 66% of the actual body weight [9 - 17]. The risk of opportunistic infections increases in patients who have significant weight loss compared to patients without weight loss [11]. Poor nutritional status can reduce the efficacy of antiretroviral treatment regimens, as some drugs may not be properly absorbed or can cause significant side effects if not taken with adequate food. In addition to the development of HIV-related diseases, the nutritional status is adversely affected by ART. Admission of some antiretroviral drugs leads to metabolic disorders. With long-term treatment, loss of fat from the face and limbs or accumulation of fat in the abdominal cavity known as lipodystrophy occurs [12, 16]. ART may also be accompanied by a disorder of lipid metabolism due to a decrease in high-density lipoprotein (HDL) and an increase in the level of low-density lipoprotein (LDL) and triglycerides in the blood, which increases the risk of cardiovascular diseases, stroke and diabetes [13]. Reviews of malnutrition in PLWH indicate that the causes are multifactorial and may be secondary to decreased dietary intake, malabsorption, metabolic disorders or endocrine dysfunction [14]. Finding the causes determines the appropriate tactics of intervention and management.

2. MATERIALS AND METHODS

This study was performed at the Federal Centre for Prevention and Control of HIV/AIDS Moscow, Russia. Forty-five asymptomatic outpatients diagnosed with HIV, the majority (85%) of which are on antiretroviral therapy and thirty-two normal healthy volunteers (control group) aged between 24 and 40, were studied between 2014 and 2016. Within the HIV group, 32 (71%) were male and 13 (29%) female. Overall their median age, CD4 count and viral load were 30 years (IQR: 28-40), 407 (IQR: 357-490) cells/mm³ and 500 (IQR: 0-1000) copies/ml, respectively. None of the participants in the HIV group had any active infection. 61% of the HIV participants received a combination of nucleoside reverse-transcriptase inhibitors (NRTIs) plus non-nucleoside reverse-transcriptase inhibitors (NNRTIs) while 39 received a combination of NRTIs plus a protease inhibitor (PI). None of the HIV study participants received NRTIs such as d4T and AZT or PIs such as saquinavir, indinavir, and ritonavir, which account for most metabolic abnormalities associated with the lipodystrophy syndrome, therefore, could alter the outcomes. Only 7 HIV participants (15%) were ART naïve. Demographic characteristics like age, gender, family and financial status, and occupational status as well as education level, lifestyle factors (increase physical activity, smoking) were obtained and there were no differences between groups. None of the study participants were reported to be food insecure. We implemented a comprehensive method which was developed at the Research Institute of Nutrition Moscow aimed at combating nutritional disorders such as cachexia and obesity. This method involves the following:

2.1. Food Intake Assessment

Evaluation of daily food intake is an important stage in assessing the nutritional status of the patient. This reflects the energy value, frequency and nutritional value of diet. During the HIV outpatient visit, data was collected using a computer Food Frequency Questionnaire (FFQ) program. The program automatically calculates macro and micronutrient consumption based on the results of the questionnaire. This dietary assessment tool (FFQ) was developed for use in the Research Institute of Nutrition Moscow. The questionnaire took on average 40 minutes to complete and included pictures of commonly eaten foods. These food items were taken from analyses of various dietary surveys conducted in urban Russia and the list included all food items eaten by the majority of the population [18]. Such an approach has been similarly implemented by researchers measuring Food and Nutrition security among HIV patients [19].

2.2. Body Composition Assessment

Data was obtained using bioelectrical impedance measurements of the body. This method is based on the principle that the electrical conductivity of the fat-free tissue mass (FFM) is far greater than that of fat. Based on the measured impedance (electrical resistance), the composition of various body structures was quantitatively evaluated, including fat and lean body mass, skeletal muscle mass, mineral substances, total, extra - and intracellular fluid. The body composition of each participant was successively measured on all applied human body composition analyzer (model InBody 720, Korea). Height, body weight and body mass index (BMI) were also determined, in addition to the calculation of the composition of the body

2.3. Metabolic Assessment

This was executed using indirect calorimetry. It measures the oxygen that the body consumes. Using this measurement, it calculates a patient's Resting Energy Expenditure (REE) and macronutrient (Fat, carbohydrate, protein) oxidation rates. Physicians can screen for abnormal metabolic rates. The urine urea nitrogen test was determined to assess the amount of protein breakdown. We evaluated biochemical metabolism markers (LDL, HDL, albumin, serum protein, glucose *etc*) were also evaluated.

2.4. Statistical Processing

Statistical processing of the results obtained during the research was carried out using Microsoft Office Excel 2007 and Statistica 8.0. The Mann-Whitney method was used to assess statistical reliability. The level of significance cut off was $p < 0.05$.

3. RESULTS

3.1. Dietary Intake Assessment

Food item and food group analyses showed similar consistency of consumption across the groups, regardless of HIV status. After a month of assessment, the majority of the HIV group (85%) had a significantly lower intake of

carbohydrates ($P < 0.01$) compared to the control group (7%) (Fig. 1). Participants in both the groups met the recommended daily allowance (RDA) level of protein requirements (90 and 65 grams for male and female HIV study participants, respectively) although, protein daily intake was high in 45% of the control group: average intake was 150 and 120 grams for male and female participants, respectively. Carbohydrate, protein, fat and fibre contributed to approximately 50%, 15%, 30% and 5%, respectively, of total energy intake in the control group while in the HIV group, carbohydrate, protein, fat and fibre contributed to approximately 35% 15%, 40% and 10%, respectively, of total energy intake (data not shown). Daily energy requirements and other vital macro and micronutrients' intake in both the groups met RDA levels.

3.2. Body Weight and Composition

Values met normal range in both groups except for free fat mass in 75% of the HIV group, which had a significantly decreased average of 7.9kg (5.1 - 9.2) in comparison to the control group ($P < 0.05$). The decrease in fat mass did not contribute to the model for the waist to hip ratio in the HIV study group as no changes were observed in comparison to the control group and the normal range. Results are indicated in Table 1 in their average values.

3.3. Metabolic And Biochemical Values

Resting energy expenditure (REE) was higher in 86% of the HIV group compared to 12% of the control group ($P < 0.05$) (Table 2). Carbohydrate oxidation rate was reduced in 88% of the HIV group in contrast to 6% of the control group ($P < 0.01$). Protein oxidation rate rose above the baseline in 77% of the HIV group compared to 3% of the control group ($P < 0.01$). An increase in fat oxidation rate was observed in 84% of the HIV compared to 6% in the control group ($P < 0.01$). Urea nitrogen concentration in urine increased in 82% of participants in the HIV group in contrast to 3% in the control group. Biochemical parameters (albumin, total protein, serum albumin, triglycerides, high- and low-density lipoprotein profile) for nutrition assessment were in normal ranges. The average values are indicated in Table 2.

4. DISCUSSION

In our study, the HIV-positive group had lower fat-free mass, although the weight and BMI, as well as lean mass and percent body met the normal range as their HIV-negative counterparts. Studies have identified that fat loss in HIV patients is associated with ARV-treatment, where lipodystrophy is characterised by abdominal fat accumulation and subcutaneous fat loss, predominantly at the face, limbs and buttocks [16, 20, 21]. These changes were not identified clinically in the HIV study group, especially among those receiving ARV-treatment. It is also important to point out

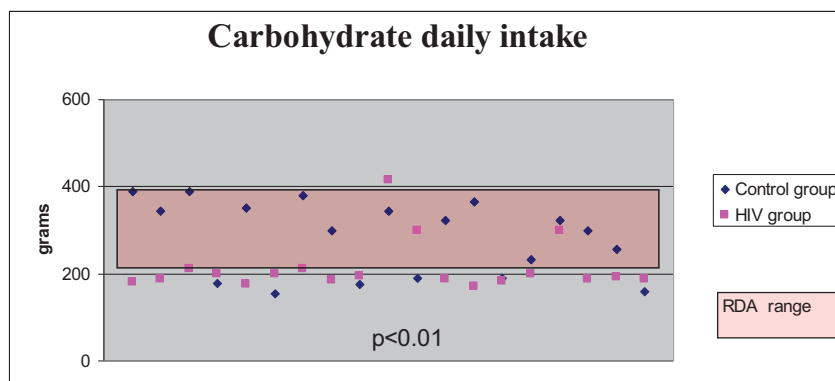


Fig. (1). Daily intake of carbohydrates in the study groups.

Table 1. Body composition variables of study groups.

Indicators	HIV group (n=45)	Control group (n=32)	HIV group vs Control group p- value	Normal range
Fat free mass kg	7.9 (5.1 - 9.2) (n=34)	15.1 (12.90 - 21.12) (n=32)	$P < 0.05$	12.8 – 20.4
Muscle mass kg	32.2 (29.1 - 35.21)	34.2 (29.99 - 35.70)		28.4 – 35.4
Body fluid, kg	37.6 (35.6 - 39.2)	35.6 (34.21 - 40.17)		36.5 – 39.1
Lean body mass (% of body weight)	74 (72.2 - 75.10)	76 (74 - 80)		68 - 86
BMI kg/m ²	22 (19.05 - 29.10)	24 (20.11 - 30.21)		18.5 – 24.9
Waist to hip ratio	0.84 (0.79- 0.91)	0.86 (0.77- 0.92)		0.75 - 0.89

n = number of participants.

Table 2. Metabolic values following indirect calorimetry.

Indicators	HIV group (n=45)	Control group (n=32)	HIV group vs Control group p- value	Normal range
Resting energy expenditure (kcal per day)	1820 (1750 - 1890) (n=39)	1817 (1772 -1860) (n=4)	P < 0.05	1470-1742
Fat oxidation rate (kcal per day %)	50 (42 - 70) (n=38)	52 (39 - 55) (n=2)	P < 0.01	30-35
Carbohydrate oxidation rate (kcal per day %)	29 (14 - 35) (n=40)	24 (22 - 29) (n=2)	P < 0.01	50-60
Protein oxidation rate (kcal per day %)	29.7 (21.22 - 32.57) (n=35)	27.7 (22.45 -31.18) (n=1)	P < 0.01	10-20
Urea nitrogen concentration in urine (gram per day)	15 (10 - 19) (n=37)	7 (6.2 - 12.17) (n=1)	P < 0.01	1- 6

n = number of participants.

that ARV drugs responsible for fat loss and redistribution were not prescribed to the HIV study participants on ARV. There was no change in the waist to hip ratio of the HIV group in comparison to the control group and normal values, which also excludes the possibility of fat redistribution usually found in HIV patients. There were no reported differences in dietary intake across study groups, with the exception of carbohydrate intake, which was lower in the HIV positive group than in the HIV negative group. Given the equal socioeconomic status, we did not relate this factor to the low carb intake. Carbohydrates contributed to approximately 35% of the total energy intake in the HIV group, which undermines the RDA recommendation of 60% [22]. Carbohydrates are a vital source of energy and they prevent protein and fats from being used as an energy source [14]. Consequently, we observed depletion of fat free mass, increased protein and fat oxidation and a marked increase in urea nitrogen concentration in urine in the HIV group reflecting protein catabolism due to lack of carbohydrate intake. The resting energy expenditure rate was higher in HIV group than in control subjects as previously documented by other studies [23, 24], so was the protein and fat oxidation rate. The WHO recommend an energy increase by 10% in adults with asymptomatic HIV to maintain body weight due to an increase in the resting energy expenditure observed in studies [25]. Dietitians at the Institute of Nutrition in Moscow (where part of the research was held) did recommend that the HIV participants adjust their dietary intake by increasing their carbs diet at RDA recommended levels to overturn the catabolic status observed. Further depletion of proteins which is a vital element for immune cells and absorption, uptake or efflux of many medications including drugs could affect the immune status of HIV patients and ARV drug efficacy. It is important to note that during our observation, the CD4 counts remained at normal limits and the viral load was undetectable. This analysis is subjected to several limitations. Firstly, the sample size was relatively small, which may have impacted the statistical power to discriminate the effects of methods implemented between the analysed groups. Secondly, because a food frequency questionnaire (FFQ) is composed of a pre-specified food list, it may not have reflected the eating patterns

of the participants, as some may have migrated to urban cities. Subsequent studies of this kind would help evaluate the nutritional and metabolic status after dietary adjustment and investigation involving two groups which comprise ARV-naïve and ARV-receiving treatment with a considerable sample size. The nutrition and metabolic status might undergo some changes given to these factors

CONCLUSION

The study demonstrated a catabolic status (negative nitrogen balance and loss of fat mass as a result of increased protein oxidation and fat oxidation rate, respectively) in the HIV study group. This was due to a reduced intake of carbohydrates, which is the main source of energy. These changes suggest an adjustment in the nutrient RDA to compensate for such status. The study also confirms an increase in the resting energy expenditure rate from previous studies. Given the results from the study, starting assessment, counselling, and education regarding nutrition shortly after HIV diagnosis is imperative. Further investigation should be extended to HIV patients with active opportunistic diseases during metabolic stress as well as in paediatric HIV infection.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Clinical Research Ethical Committee of the Federal Centre for Prevention and Control of HIV/AIDS Russia, Russia (Reference No.54).

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Written informed consent for publication was obtained by all study participants.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of the article is available at <http://www.crie.ru/autoref.ht>, reference number 208.114.01.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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