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Dietary pattern association with CD4 cells count in patients living with human immunodeficiency virus: A cross-sectional study

Parisa Keshani[1], Sorour Sarihi[2,4], Narges Parsaie[3] and Hassan Joulaei[3]

Abstract

Background: Considering contradictory reports about the impact of dietary pattern on CD4 cell count in previous studies and the potential importance of diet on the immune system, this study aimed to assess the association between dietary patterns and CD4 count among HIV-infected patients.

Methods: This cross-sectional study was conducted among HIV-infected patients aged 18–60 who registered in the referral Voluntary Counseling and Testing Center of Shiraz, Iran. The principal component analysis identified nutritional patterns and factors. The association between the score of the dietary patterns and CD4 count was considered in two categories of CD4 more/less than 500 and using backward logistic regression after adjusting for confounders.

Results: A total of 226 participants were included in the analysis. CD4 was significantly lower in males ($p < 0.001$). Participants with illegal drug use ($p < 0.001$), HCV ($p = 0.001$), and HBV ($p < 0.001$) had lower serum CD4. Four extracted dietary patterns were a Plant-rich diet, Healthy animal-based proteins, a Western diet, and Affordable calorie and protein patterns. There was an association between CD4 and Western diet patterns in the best model in which age, gender, weight, and HBV were included. Each unit increase in Western diet score increased the odds of CD4 less than 500 by 57% (OR = 1.57; CI 95% 1.06–2.34, $p = 0.02$).

Conclusion: Among the four dietary patterns, the Western diet comprising a high intake of refined sugar and grain, saturated and trans fats, and animal protein sources, especially high-fat red meat, had a statistically significant relationship with a decrease in CD4 cell count.

Keywords

AIDS, CD4 lymphocyte count, dietary pattern, HIV, Western diet

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Introduction

Approximately 38.0 million people were living with the human immunodeficiency virus (HIV) in 2019, and 1.7 million people were newly infected with HIV in the same year.[1] In 2018, estimates showed that nearly 61,000 people were living with HIV in Iran.[2] HIV can cause several health complications, including opportunistic infections, oxidative stress, wasting syndrome, and malnutrition.[3–5] Many metabolic changes occur in people living with HIV (PLWH). HIV damages the immune system by targeting CD4 cells. A low CD4 count indicates HIV has weakened the immune system.[6] HIV treatments

[1]Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Department of Human Nutrition and Hospitality Management, College of Human Environmental Sciences, The University of Alabama, Tuscaloosa, AL, USA
[3]HIV/AIDS Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran
[4]Alabama Research Institute on Aging(ARIA), The University of Alabama, Tuscaloosa, AL, USA

Corresponding author:
Hassan Joulaei, HIV/AIDS Research Center, Institute of Health, Shiraz University of Medical Sciences, Lavan Street, Shiraz, Fars, P.O. Box 7165983885, Iran.
Email: joulaei_h@yahoo.com

such as anti-retroviral therapy (ART) strengthen the immune system and extend the life of these patients. However, weight loss or lean body mass and wasting were associated with an increased risk of opportunistic infection and death in PLWH.[6,7] Malnutrition undermines the patient's immune system and increases susceptibility to other diseases, exacerbating malnutrition and weakening the immune system.[5] Resting energy expenditure increases in PLWH, although factors such as inflammatory cytokines and secondary infections seriously affect appetite, food intake, and weight.[6] Several studies have shown increased levels of inflammation biomarkers in HIV-infected patients and their association with increased risk of poorer outcomes and all-cause mortality.[8–12]

Although body composition and biochemical measures of metabolic risk were extensively investigated in HIV, the role of diet has received less attention. Several studies[7,13,14] investigated the effect of nutrients on dietary intake. Although necessary, the association of individual nutrient intake with disease outcomes can be challenging to detect because nutrients are not consumed in isolation. Consequently, dietary pattern analysis seems to be a promising way to assess the effect of total food consumption on the immune system of PLWH. The dietary pattern could be defined as an essential determinant of the overall nutrient intake, nutritional status, and health among the target groups of individuals or populations.[15] Studies have confirmed that healthy dietary choices improved the quality of life (QoL) and the anthropometric status of adults living with HIV.[8] Although it remains uncertain the extent to which poor nutritional quality influences an individual's susceptibility to HIV infection, it is widely agreed that the progression of AIDS and response to therapy is affected by diet.[16] Therefore, ensuring HIV-infected individuals have access to high-quality, nutritious food choices that promote optimal dietary patterns, rather than just sufficient quantities of food, will also be increasingly important. HIV-infected individuals must follow a healthy, nutritious, and adequate diet to boost their immunity against opportunistic infections and avoid muscle wasting. Poor nutritional status is likely to affect disease outcomes adversely.[17]

In several studies, improving micronutrient status has been shown to associate with lower mortality, aging, and improved CD4 cell count.[12,16,18–22] On the other hand, reviews by Irlam et al.[23] and Grobler et al.[24] found no conclusive evidence that micronutrient and macronutrient supplementation effectively reduces morbidity or mortality in people with HIV infection.

The lack of knowledge limits efforts in providing more precise dietary guidance to reduce metabolic risk among HIV-infected patients. Due to the lack of literature and contradictory results on the effects of dietary patterns on CD4 cell count and the immune system,[25,26] the present study aimed to assess the association between dietary patterns and CD4 counts as the primary marker to detect the immune system health among people infected with HIV.

Method

Study setting and participants

This cross-sectional study was conducted among HIV-infected patients referred to Voluntary Counseling and Testing Center (VCT), Shiraz, Iran. There were 1804 registered medical records in the center, in which 1335 files were active. The participants have been selected from the active files referred to the AIDS Research Center, who came monthly to receive medicine and perform tests.

Regarding the maximum possible food groups (25 food groups) and 5–10 participants per food group[27] to determine the dietary pattern using factor analysis, a sample size of 250 people was determined.

Inclusion and exclusion criteria

Adults aged 18–60 receiving ART, with active medical files in the VCT center, who had visited the center to receive medicine and perform routine tests, were included using a convenience sampling method. Participants with a mental disability or hangover were not included due to their inability to complete the questionnaire.

Measurement of anthropometric and other variables

A socio-demographic questionnaire was completed by each participant in an interview to assess their age, gender, marital status, educational level, occupational status, smoking habits, drug abuse, socioeconomic status, living costs, and physical activity level. Information such as medications received, disease history, including Hepatitis C Virus (HCV) and Hepatitis B Virus (HBV), depression history, and CD4 count was collected from the most recent medical records completed by the physician of the VCT Center; and anthropometry measurements were performed the same day by the same physician and the same tool, as part of the center's routine services.

Dietary assessment

A valid and reliable semi-quantitative 168-item food frequency questionnaire (FFQ) was used to evaluate dietary intake. The standard serving size commonly consumed by Iranians was considered. Participants were asked to report their consumption frequency of an intended serving of each food item during the last year, daily, weekly, monthly, or annually. Then, each food item was converted into a daily intake. Due to the lack of sufficient vitamin D levels in Iranian food and restriction of daily dietary intake of this micronutrient from the natural origin,[28] serum vitamin

D was measured (using ELIZA kit-IDEAL Tashkhis Atieh co) as a covariate. Based on their similarity in nutritional composition, food items were classified into 16 groups (Supplemental File 1). The primary dietary patterns were determined by Principal Component Analysis (PCA).

Statistical analysis

In the present study, CD4 and dietary pattern scores were dependent and independent variables, respectively. Data were analyzed using SPSS (version 25; SPSS Inc., Chicago, IL, USA) by running the student's t-test for normally distributed variables and chi-squared tests for categorical variables. Quantitative and qualitative variables were expressed as mean $\pm$ SD and percentage. The dietary patterns were identified by PCA. In this study, the sampling and data collection sufficiency was approved by KMO values >0.6 and $p \leq 0.05$ for Bartlett's test of sphericity. Factors with an eigenvalue of 1.0 or more were retained for further investigation. The scree plot was used to decide on another approach. To simplify the data interpretation, orthogonal rotation (varimax) was applied.

The analysis included food groups with a factor loading of $\geq \pm 0.3$. The patterns were named based on the highest factor loadings on each pattern. The association between the score of 4 of dietary patterns and CD4 (in two categories of CD4 $<$ 500 and CD4 $\geq$ 500)[29] was calculated by odds ratio (OR) and the 95% confidence intervals (CIs) using binary logistic regression and the backward method. CD4 $\geq$ 500 was considered as a reference group in statistical analysis. Variables, including age, gender, marital status, education, job, weight, smoking, illegal drug use, physical activity, and HBV and HCV positivity, with *p*-values less than 0.2 in univariable analysis, were included in the multivariable analysis as confounders.

Ethics declarations

The Shiraz University of Medical Sciences Ethics Committee confirmed the study protocol based on the 1975 ethical guidelines of Helsinki's declaration (ethics code: IR.SUMS.REC.1397.1282). The purposes of this study were explained to all participants and their companions, such as their spouses or parents. Illiterate participants were asked to sign an informed consent with the help of their guardians, and educated participants provided their own signatures on written informed consent.

Result

The dietary information of 24 participants was excluded because their energy intake was more or less than 3, as a standard deviation from the mean on the log-transformed scale. A total of 226 participants were included in the analysis; 133 (59.0%) were male, and the mean age of the sample was 43.51 $\pm$ 9.12. Table 1 shows the participants' demographic characteristics based on their CD4 count.

Serum CD4 was categorized into two groups of $<$500 and $\geq$500.[30] CD4 was significantly lower in men ($p < 0.001$); and participants with illegal drug use ($p < 0.001$). Participants with HCV ($p = 0.001$); and HBV ($p < 0.001$) also had lower serum levels of CD4. Participants with CD4 $<$ 500 had higher age ($p = 0.001$) and lower weight ($p = 0.001$) on average. Other variables, such as socioeconomic parameters and energy intake, were not significantly different between the two groups.

Four nutritional patterns were distinguished based on the analysis of the eigenvalue and scree plot (Supplemental File 2). The first pattern was named the vegan diet, identified by a high intake of fruit and fruit juice, green vegetables, orange vegetables, olives, beans, and nuts. The second pattern was the normal animal-based proteins identified by a high intake of dairy products, white meats, tuberous vegetables, onion, garlic, and spices. The third dietary pattern was Western, characterized by high amounts of grains, especially refined grains, sweet snacks, and red and processed meat. The fourth pattern was affordable calorie and protein characterized by high amounts of egg, potato, fat, and oil. The list of food groups and their factor loadings are included in Table 2. These dietary patterns explained 47.96% of the total variance. The association between CD4 and adjusting confounders of nutritional patterns are summarized in Table 3. The association between CD4 cell count and vitamin D serum levels was non-significant. Variables, including age, gender, weight, HBV, and Western diet pattern, encompassed the last model in a backward logistic regression. There was a positive association between the Western diet and having CD4 $<$ 500 (low immunity). Western diet increased odds of CD4 $<$ 500 by 57% (OR = 1.57; 95% CI 1.06–2.34, $p = 0.02$) and weight by 3% (OR = 1.03; 95% CI 1.01–1.05, $p = 0.006$). Women (OR = 0.28; 95% CI 0.14–0.55, $p < 0.001$) were more likely to be in the lower CD4 group than men, and there was an inverse association between age (OR = 0.95; 95% CI 0.92 and 0.99, $p = 0.01$) and risk of lower CD4 in this study.

Discussion

This study primarily intended to determine the association between CD4 cell counts in HIV patients and nutritional patterns. In this cross-sectional survey of adult patients with HIV/AIDS undergoing drug treatment, we identified four distinct dietary patterns: vegan, healthy animal-based protein, affordable calorie & protein, and western diet types. The findings showed that the western diet pattern was associated with the CD4 cell count in HIV-infected patients, and as the diet score increased, the ratio of CD4 cell count $<$500 would increase by 57%.

Table 1. Characteristics of participants based on CD4 count.

	CD4 < 500	CD4 ≥ 500	
	N = 137	N = 89	*p*-Value
	n (%)	*n* (%)	
Gender			<0.001
Female	42 (29.9)	51 (56.2)	
Male	95 (68.6)	38 (42.7)	
Education			0.19
Illiterate	4 (2.9)	3 (3.4)	
Primary school	57 (49.9)	27 (29.2)	
Less than diploma	42 (29.9)	34 (37.1)	
Diploma and undergraduate	31 (21.9)	18 (20.2)	
Graduate	3 (2.2)	7 (7.8)	
Marital status			0.09
Single	39 (28.5)	15 (16.9)	
Married	66 (47.4)	46 (50.6)	
Divorced/widow	32 (22.6)	28 (31.5)	
Employment status			0.06
Unemployed	70 (50.4)	56 (61.8)	
Employed	67 (48.2)	33 (37.1)	
SES			0.72
Poor	104 (74.5)	69 (75.3)	
Moderate	29 (21.2)	16 (18.0)	
Fair	4 (2.9)	4 (4.5)	
Living cost			0.25
<2 million (100 $)	111 (82.4)	67 (77.8)	
>2 million (100 $/month)	26 (17.6)	22 (22.2)	
Smoking			0.09
Yes	74 (53.3)	39 (43.8)	
No	63 (45.3)	50 (55.1)	
Illegal drug use			0.006
Yes	40 (28.5)	12 (13.5)	
No	97 (70.1)	77 (85.4)	
Depression history			0.32
Yes	14 (9.5)	7 (6.9)	
No	123 (88.3)	82 (93.1)	
Physical activity			0.17
Sedentary	39 (27.7)	22 (24.7)	
Low activity	55 (39.4)	47 (51.7)	
Moderate and vigorous activity	43 (31.4)	20 (22.7)	
HCV			0.001
Yes	76 (54.7)	29 (32.6)	
No	61 (43.1)	60 (66.3)	
HBV			<0.001
Yes	17 (10.9)	0	
No	120 (86.1)	89 (100)	
Vitamin D3			0.02
Deficiency ≤20 ng/l	24 (17.5)	29 (31.5)	
Insufficiency 21–29 ng/l	45 (32.8)	19 (21.3)	
Normal ≥30	68 (48.9)	40 (43.8)	
	Mean ± SD	Mean ± SD	
Age	41.05 ± 9.78	45.18 ± 8.23	0.001
Weight	68.10 ± 13.63	62.26 ± 12.68	0.001
Disease duration	7.67 ± 5.55	7.38 ± 4.74	0.69
Energy intake	2370.78 ± 853.03	2420.48 ± 899.24	0.67
Protein intake	77.19 ± 28.96	79.69 ± 33.56	0.57

HBV: Hepatitis B virus; HCV: Hepatitis C virus; SES: socioeconomic status.

In congruence with our findings, previous studies have shown the western diet pattern characterized by high consumption of energy-dense foods with relatively high amounts of fat, animal protein, refined grains, sugar, and sweets; adversely affects the treatment outcome and quality of life among adult patients with HIV.[31,32] Several mechanisms have been proposed to explain persistent inflammation during HIV infection. A widely accepted mechanism was increased intestinal permeability due to the loss of mucosal $CD4^+$ T cells during early infection with HIV.[9] Thus, the Western diet may reduce CD4 count, thereby increasing intestinal permeability and exacerbating inflammation. Also, sugar, as a prominent part of the Western diet pattern,[25,26] impacts health status of HIV-infected patients too. According to observational reports, dietary sugar intake (specifically, sugar-sweetened beverages) could stimulate subclinical inflammation. The potentially relevant mechanism is the promotion of de novo synthesis of free fatty acids (FFA) in the liver by dietary sugar.[33–35] According to the lipotoxicity theory, FFA metabolites may trigger inflammatory processes and the formation of reactive oxygen species (ROS) as measured by the inflammatory marker C-reactive protein (CRP). Most Western diet foods, including refined sugar and saturated fats, activate the inflammatory mechanism and increase inflammatory cytokines in patients.[34,35] Our results align with another study in Malawi on a population of pregnant women infected with HIV.[36]

Annan et al.'s[36] study showed a strong association between animal-based dietary patterns and micronutrient intake in HIV individuals. These studies suggested that inadequate nutritional intake (reduced or increased food intake) impacts the immune system, which is of substantial importance among HIV-infected patients.[31,36]

Nutritional status can affect the overall health and longevity of PLWH. Several epidemiologic studies investigated the impact of being underweight or overweight on the nutritional status of HIV-infected patients. Some reported the prevalence of malnutrition as up to 42.2%.[31]

As the body continually utilizes micronutrients, including iron, copper, selenium, and zinc, as vital components of the enzymes involved in immunity, these micronutrients must be ingested regularly. The impact of nutrient deficiencies is greater for PLWH compared to individuals without HIV/AIDS.[37,38] Micronutrient deficiencies will exacerbate protein malnutrition. The level of oxidative stress in these patients favors disease progression and mortality. In the present study, patients with lower average weight had higher odds of CD4 cell count <500 by 3%. Nutritional interventions should be individualized according to the problems identified. Plans include achieving healthy body weights, body composition, and improved laboratory values.

Our findings confirmed that the average age of HIV-infected patients was significantly higher in groups with of CD4 cell count of >500, which could be due to more

Table 2. Rotated factor loadings for the four dietary patterns.

	Vegan diet	Healthy animal-based proteins	Western diet	Affordable calorie and protein
Fruit and fruit juice	0.755			
Green vegetables	0.741			
Olive and olive oil	0.603			
Beans and nuts	0.571			
Orange veg	0.547			
Tuberous vegetables		0.672		
Onion, garlic, seasonings, spices		0.642		
Dairy products		0.604		
White meat		0.581		
Sweetened beverages, soft drinks, and soda			0.773	
Grains			0.693	
Sweet snacks			0.610	
Red meat and processed meat			0.371	
Egg				0.784
Potato all kinds				0.758
Fats and oils				0.548

Table 3. Odds ratio and 95% confidence interval for the association between dietary pattern and CD4 count.

	β	SE	Exp(β)	95% CI for Exp(β) Lower–Upper	*p*-Value
Crud model					
Vegan diet	0.36	0.21	1.43	0.94–2.17	0.08
Healthy animal-based proteins	0.28	0.16	1.33	0.97–1.82	0.07
Western diet	−0.01	0.17	0.98	0.70–1.38	0.93
Affordable calorie and protein	−0.14	0.15	0.86	0.63–1.17	0.34
Best model					
Western diet pattern	0.45	0.21	1.57	1.06–2.34	0.02
Age	−0.04	0.01	0.95	0.92–0.99	0.01
Gender (female)	−1.26	0.34	0.28	0.14–0.55	<0.001
Weight	0.03	0.01	1.03	1.01–1.05	0.006
HBV (yes)	0.33	0.43	1.39	0.584–3.33	0.45

β: β coefficient; CI: confidence interval; HBV: Hepatitis B virus; SE: standard error.

self-care in older adults. However, a cohort study found no significant difference in age, sex, disease stage, and CD4 cell count among patients with and without anemia.[39] Our research indicated a significant association between patients' gender and CD4 cell count. Also, the frequency of HIV-infected men with CD4 cell count <500 was higher.

Some studies have reported a potential protective role for vitamin D among HIV-infected patients.[33–35,40,41] Despite reported vitamin D deficiency among HIV-positive patients in Iran[16] and other countries,[42,43] numerous studies, like our survey, indicated no significant association between CD4 cell count and vitamin D serum levels.[44–46] The principal reason is overall vitamin D deficiencies in HIV-infected patients and the Iranian population in general.[16,36,47,48] Furthermore, there are many non-HIV-related risk factors for Vitamin D deficiency, including sex, advanced age, limited sunlight exposure, low levels of dietary Vitamin D intake, gastrointestinal absorption disorders, hepatic and renal diseases, higher body mass index, diabetes mellitus, and alcohol consumption.[42,43]

We found no significant correlation between education level, marital status, employment status, smoking, medication usage, physical activity levels, depression history, disease duration, economic condition, participants' average energy and protein intake, and CD4 cell count. As demonstrated in previous studies, socioeconomic status, food security, education level, and employment play substantial roles in food supplies and energy or overall food intake.[49,50] We did not find a statistically significant association between the participants' energy and protein intakes and CD4 cell count because there were no differences between the participants regarding education level, economic condition, and employment status. Therefore, we could not expect differences between their average protein and energy intake. Moreover, there was a significant relationship between drug abuse, HCV- and HBV-infected patients, and the CD4 cell count of HIV-positive participants.

Nutritional status may affect HIV-infected patients' overall health and longevity.[6,12] Goals for dietary interventions should be individualized according to the problems identified. Although food patterns provide a holistic view of the diet,[15] limited studies have been conducted to determine the nutritional patterns of HIV-infected patients in Iran.

It seems a balanced food pattern, as an alternative and beneficial option, could effectively regulate energy intake homeostasis in these patients. A future case-control or cohort study would confirm the association between CD4 and the patient's nutritional pattern. Measuring serum levels of other micronutrients involved in immune activities, including zinc, selenium, and vitamin A could provide additional evidence. There are no specific guidelines for nutritional counseling in HIV/AIDS-infected patients in Iran. Due to the effect of nutritional and dietary patterns on immunity and CD4 counts, nutritional counseling is indicated as part of the treatment guidelines for these patients.

Conclusion

From the four dietary patterns examined in this study, the Western diet containing a high intake of refined sugar, saturated and trans fats, and animal protein sources, especially high-fat red meat and refined grains, was statistically significantly associated with a decrease in CD4 cell count by 57%.

Nutritional education and training on healthy dietary patterns among HIV/AIDs-infected patients could increase immunity via CD4 improvement and lessen their quality of life. Further studies are needed to investigate the best dietary pattern for boosting immunity among these patients.

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Author contributions

HJ was responsible for the study concept and design, critical revision of the manuscript for intellectual content, administrative, technical, and material support, and study supervision. SS acquisition of data, analysis and data interpretation, drafting of the manuscript, and critical revision of the manuscript for intellectual content. PK was responsible for the study concept and design, study supervision, analysis and interpretation of the data, drafting of the manuscript, critical revision for intellectual content, and statistical analysis. NP was responsible for data collection, drafting the manuscript, and critical revision of the manuscript.

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Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Supplemental material

Supplemental material for this article is available online.

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