ISSN: **2764-4006** | www.revistacientificaipedss.com

HIV, CHRONIC INFLAMMATION AND NUTRITION: RELATIONSHIP BETWEEN DIET, INFLAMMATORY MARKERS, AND METABOLIC DI - SEASES - INTEGRATIVE REVIEW WITH A SYSTEMATIZED APPROACH

Lismeia Raimundo Soares
Corresponding e-mail: lismeia@gmail.com
Publication date: April 29, 2026
DOI: http://doi.org/10.55703/27644006060119

ABSTRACT

HIV infection has come to be understood as a chronic condition requiring long-term management following the expansion of antiretroviral therapy. However, even in individuals with viral suppression, residual systemic inflammation remains associated with increased non–AIDS-defining morbidities, metabolic alterations, and cardiovascular risk. This integrative review with a systematic approach aimed to analyze the scientific evidence on the relationship between HIV, chronic inflammation, and nutrition, with an emphasis on the association between diet, inflammatory markers, the intestinal microbiota, and metabolic diseases. Twenty-six real and traceable studies were included, covering critical reviews, observational studies, cohorts, clinical trials, multi-omics analyses, systematic reviews, and meta-analyses. The findings showed that biomarkers such as IL-6, C-reactive protein, D-dimer, sCD14, sCD163, TNF-alpha, TNFR1, LPS, and I-FABP are related to persistent immune activation, microbial translocation, cardiovascular risk, and metabolic syndrome in people living with HIV. Poor diet quality, reduced intake of fruits, vegetables, and fiber, as well as food insecurity, have been associated with greater inflammatory and metabolic vulnerability. On the other hand, healthier dietary patterns—especially those close to the Mediterranean diet—along with interventions using extra-virgin olive oil, omega-3, and DHA, showed potential to modulate lipid, oxidative, microbial, and inflammatory parameters, although the effects are not uniform across all markers. It is concluded that nutrition plays a strategic role in the comprehensive care of people living with HIV and should be integrated into virologic control, metabolic monitoring, assessment of body composition, and addressing food insecurity.

Keywords: hiv; chronic inflammation; nutrition; metabolic diseases.

ISSN: **2764-4006** | www.revistacientificaipedss.com

INTRODUCTION

Human immunodeficiency virus (HIV) infection has undergone profound clinical transformation over the past decades, especially after expanded access to antiretroviral therapy (ART). Sustained control of viral replication has led to a marked increase in survival and a reduction in opportunistic infections and AIDS-defining events. However, even in individuals with suppressed viral load, HIV infection remains associated with a state of persistent immune activation, residual systemic inflammation, and a higher occurrence of chronic noncommunicable comorbidities, including cardiovascular diseases, metabolic alterations, liver disease, renal impairment, osteopenia, neuroinflammation, and early clinical frailty [1,2].

Chronic inflammation in HIV is considered a multifactorial phenomenon, arising from the interaction between residual viral persistence, activation of immune cells, intestinal barrier dysfunction, microbial translocation, alterations in the microbiota, coinfections, immunological aging, and metabolic effects related to ART itself [1,3,4]. Classic studies have shown that biomarkers such as interleukin 6 (IL-6), High-sensitivity C-reactive protein (hs-CRP), D-dimer, sCD14, and sCD163 have prognostic relevance in people living with HIV, being associated with mortality, cardiovascular events, and non-AIDS-defining morbidities [2-4]. Thus, clinical follow-up of this population cannot be limited to CD4+ T-lymphocyte counts and viral load; it is necessary to understand the inflammatory, metabolic, and nutritional mechanisms that influence long-term health.

Among the main outcomes associated with persistent inflammation in HIV, metabolic and cardiovascular diseases stand out. People living with HIV have a higher frequency of dyslipidemia, insulin resistance, alterations in body composition, lipodystrophy, metabolic syndrome, and increased cardiovascular risk [3,24,25]. These phenomena are influenced by multiple factors, including chronic inflammation, endothelial activation, changes in adipose tissue, specific effects of certain antiretroviral regimens, aging, and lifestyle [3,25]. In this context, metabolic syndrome assumes particular clinical relevance because it represents the convergence of changes such as abdominal obesity, hypertension

arterial, hyperglycemia, hypertriglyceridemia and reduced HDL cholesterol, factors that can intensify the risk of cardiovascular events in individuals with HIV [24].

Nutrition emerges as a strategic component in this scenario, since the quality of the diet can directly influence pathways metabolic,

inflammatory, oxidative, and immunological. Studies have shown that people living with HIV often have inadequate dietary patterns, with low intake of fruits, vegetables, fiber, dairy, and foods with an anti-inflammatory profile, as well as higher consumption of saturated fats and ultra-processed foods in certain contexts [5-7]. Poor dietary quality can worsen cardiometabolic risk, contribute to intestinal dysbiosis, and favor the maintenance of a chronic inflammatory environment. On the other hand, dietary patterns more healthy,

especially those close to the Mediterranean diet have been associated with a better metabolic profile, a more favorable composition of the gut microbiota, and a possible reduction in inflammatory biomarkers [8,9,11].

The relationship between diet, inflammation, and HIV should also be understood from the gut axis, microbiota, and immunometabolism perspective. The intestinal mucosa is one of the main sites of early immune injury during HIV infection, with loss of integrity of the epithelial barrier, reduced local immune surveillance, and increased passage of microbial products into the systemic circulation [1,26]. This process, known as microbial translocation, may stimulate monocytes, macrophages, and other immune system cells, contributing to elevated markers such as LPS, sCD14, I-FABP, and pro-inflammatory cytokines [13,26]. Changes in the gut microbiota have been associated with inflammation, cardiovascular risk, metabolic syndrome, and hepatic alterations in people living with HIV [12-15].

In this sense, diet may act as a modulator of the gut microbiota and the inflammatory response. Studies on the Mediterranean diet, extra virgin olive oil, fibers, agrarian dietary patterns, and supplementation with omega-3 fatty acids suggest that nutritional interventions may have effects on lipid profile, oxidative stress, inflammatory biomarkers, and microbial composition [8,9,16-21].

However, the results are not yet completely homogeneous. Some interventions show benefit in markers such as CRP and lipid parameters, while others show no significant association with IL-6, TNFa-lfa, intestinal permeability, or systemic inflammation markers [10,20,21]. This indicates that the effects of nutrition on HIV may vary according to the individuals' clinical, immunological, metabolic, dietary, and microbiological profiles.

In addition to biological and dietary aspects, food insecurity is a relevant social determinant of chronic inflammation in people living with HIV. Difficulty accessing adequate food regularly may compromise adherence to therapy, worsen diet quality, promote metabolic alterations, and intensify immune activation [22,23]. Studies have shown an association between food insecurity and increased levels of IL-6, TNFR1, sCD14, sCD 27, and sCD163, suggesting that social and nutritional vulnerabilities may contribute to the persistence of inflammation and to a higher risk of chronic diseases in this population [22,23]. Therefore, the nutritional approach in HIV must go beyond the analysis of isolated nutrients, incorporating socioeconomic conditions, access to food, dietary pattern, and metabolic risk.

Despite advances in the evidence, there are still important gaps regarding the relationship between diet, inflammatory biomarkers, and metabolic diseases in people living with HIV. Some of the studies have a cross-sectional design, small samples, or heterogeneity in terms of the biomarkers assessed, nutritional interventions, antiretroviral regimens, and the clinical characteristics of participants. In addition, most of the evidence points to relevant associations, but there is still a need to better understand causality, dose-response relationships, the ideal duration of nutritional interventions, and subgroups with the greatest potential for benefit [10, 11,20,21].

Given this context, this integrative review with a systematic approach aims to critically analyze the scientific evidence on the relationship between HIV, chronic inflammation, and nutrition, with an emphasis on the influence of diet, inflammatory markers, the intestinal microbiota, and metabolic diseases in people living with HIV. It also seeks to understand how dietary patterns, food insecurity, and

specific nutritional interventions cardiometabolic risk and outcomes can modulate systemic inflammation, the clinicians in this population.

METHODOLOGY

This is an integrative literature review with a systematized approach, developed with the aim of gathering, analyzing, and synthesizing scientific evidence regarding the relationship between HIV, chronic inflammation, and nutrition, with emphasis on the association between diet, inflammatory markers, the gut microbiota, microbial translocation, metabolic diseases, and cardiometabolic risk in people living with HIV. The choice of an integrative review is justified by the breadth of the phenomenon investigated, which involves different methodological designs, including narrative and mechanistic reviews, observational studies, cohorts, clinical trials, nutritional intervention studies, multi-omics analyses, systematic reviews, and meta-analyses. The systematized approach was adopted to provide greater transparency, organization, and rigor to the process of identifying, selecting, extracting, and interpreting the studies, without restricting the analysis to a single type of methodological design.

The preparation of the review was guided by previously defined steps, including formulating the guiding question, defining descriptors and search terms, selecting the scientific databases, establishing eligibility criteria, screening the studies, standardized data extraction, and narrative synthesis of the findings. As a complementary methodological reference, principles from the PRISMA 2020 checklist were considered, especially with regard to transparency in study identification, screening, eligibility, and inclusion. However, since this is an integrative review with a systematized approach, the synthesis of results was conducted in a narrative and thematic manner, allowing the integration of quantitative, qualitative, mechanistic, and clinical evidence.

The guiding question defined for this review was: what scientific evidence exists regarding the relationship between diet, inflammatory markers, and metabolic diseases in people living with HIV? Based on this question, an attempt was made to understand how the quality of the

Diet, dietary patterns, food insecurity, the gut microbiota, microbial translocation, and nutritional interventions are related to chronic inflammation, immune activation, metabolic changes, metabolic syndrome, and cardiovascular risk in this population.

The literature search was structured using controlled descriptors and free terms related to the topic, combined using Boolean operators. English terms were used, considering the greater availability of studies indexed internationally, including: HIV, human immunodeficiency virus, chronic inflammation, immune activation, diet, diet quality, nutrition, Mediterranean diet, omega-3 fatty acids, food insecurity, gut microbiota, microbial translocation, inflammatory biomarkers, IL-6, C-reactive protein, D-dimer, sCD14, metabolic syndrome, cardiovascular risk, dyslipidemia, insulin resistance, and antiretroviral therapy. The search strategies were adapted according to the specificities of each database, using combinations such as: HIV AND chronic inflammation AND nutrition, HIV AND diet quality AND inflammatory biomarkers, HIV AND gut microbiota AND metabolic syndrome, HIV AND food insecurity AND immune activation, HIV AND omega-3 AND inflammation, HIV AND Mediterranean diet AND microbiota, and HIV AND antiretroviral therapy AND metabolic alterations.

Recognized scientific databases and sources were consulted, including PubMed/MEDLINE, PubMed Central, PLOS, Frontiers, MDPI, Oxford Academic, BMC/Springer, Clinical Nutrition, and journals indexed in international biomedical databases. The search prioritized studies published in peer-reviewed journals, with available bibliographic information traceable, including title, authorship, journal, year of publication, volume, issue, pages or electronic identifier, DOI, PMID, or PMCID when available. The traceability of the studies was considered an essential criterion for inclusion in the final review database.

Studies were included that addressed, directly or indirectly, the relationship between HIV, chronic inflammation, diet, nutrition, gut microbiota, inflammatory markers, microbial translocation, metabolic diseases, metabolic syndrome, dyslipidemia, insulin resistance, or cardiovascular risk. Different methodological designs, including

critical reviews, cross-sectional studies, observational studies, cohorts, randomized clinical trials, nutritional intervention studies, multi-omics analyses, systematic reviews and meta-analyses. Studies on food insecurity in people living with HIV were also considered, provided they showed an association with immune activation, systemic inflammation, or the risk of chronic diseases. The inclusion of studies with different designs was necessary due to the multifactorial nature of the topic and the need to integrate clinical, metabolic, and immunological evidence, nutritional and microbiological.

Studies that did not present a clear relationship with people living with HIV, articles without adequate bibliographic traceability, publications without peer review, editorials without direct scientific contribution to the review's objective, studies exclusively focused on acute malnutrition without analysis of inflammation or metabolism, research centered only on adherence to ART without an interface with nutrition or inflammation, studies on pediatric HIV when not comparable to the adult population, and articles that addressed metabolic diseases without establishing a link to inflammation, diet, microbiota or antiretroviral therapy. Duplicate records were also excluded, as were studies with insufficient bibliographic information and publications whose content did not align with the proposed thematic axis.

Study selection took place in successive stages. Initially, potentially relevant publications were identified using the search strategies. Next, the titles and abstracts were screened to verify alignment with the review topic. The eligible studies were then subjected to full-text review or to expanded bibliographic information available in scientific databases. After this step, a final database was compiled with 26 real, traceable studies aligned with the review objective. The final selection sought to ensure a balance between classic studies on chronic inflammation in HIV, evidence on diet quality, research on microbiota and microbial translocation, studies on nutritional interventions, investigations related to food insecurity, and publications on metabolic syndrome and metabolic changes associated with ART.

Data extraction was performed using a standardized matrix,

contemplating the following information: author and year of publication, type of study, population or sample, variables or markers analyzed, main findings, and the study's contribution to the review. The inflammatory and metabolic markers of greatest interest included IL-6, C-reactive protein, ultrahigh-sensitivity C-reactive protein, D-dimer, sCD14, sCD163, TNF-alpha, TNFR1, LPS, IFABP, lipid parameters, blood glucose, insulin resistance, body composition, metabolic syndrome, gut microbiota, and dietary quality indicators. Data regarding dietary patterns, the Mediterranean diet, consumption of extra-virgin olive oil, supplementation with omega-3 fatty acids, food insecurity, and antiretroviral therapy regimens were also extracted.

Data analysis was conducted through narrative synthesis and thematic categorization. After a critical reading of the studies, the findings were grouped into six main axes: chronic inflammation, coagulation, and non–AIDS-defining events; diet quality and dietary patterns; gut microbiota, translocation microbial and immunometabolism; nutritional interventions and inflammatory modulation; food insecurity and immune activation; and metabolic syndrome, risk cardiovascular and antiretroviral therapy. This organization enabled the integration of evidence of different types and the identification of convergences, divergences, and gaps in the literature.

Because this is an integrative review based on secondary data from studies previously published and available in scientific databases, there was no need for submission to an Ethics Committee for Research, in accordance with applicable rules for research that does not involve direct data collection with human beings. Even so, the principles of scientific rigor, transparency methodological, traceability of sources, fidelity to the findings of the original studies, and proper use of references in Vancouver style.

RESULTS

This integrative review with a systematized approach included **26 studies** published between 2008 and 2026, encompassing different methodological designs and levels of evidence. The analyzed base brought together critical reviews, studies cross-sectional, studies observational studies, cohorts, clinical trials, nutritional intervention studies, multiomics analyses, reviews

systematic reviews and meta-analyses. This methodological diversity allowed a broad understanding of the relationship between HIV, chronic inflammation, nutrition, intestinal microbiota, inflammatory markers, and metabolic diseases.

The included studies showed that chronic inflammation in people living with HIV cannot be understood solely as a direct consequence of viral replication. Even in individuals receiving antiretroviral therapy and with viral suppression, there is persistence of systemic immune activation, changes in the intestinal barrier, microbial translocation, dysbiosis, metabolic alterations, and increased risk of non–AIDS-defining events [1-4,26]. The biomarkers most frequently associated with this process were IL-6, C-reactive protein, ultrasensitive C-reactive protein, D-dimer, sCD14, sCD163, TNF-alpha, TNFR1, LPS, and IFABP [2-4,22,23,26].

The analysis of the studies made it possible to organize the findings into six main areas: chronic inflammation and non–AIDS-defining events; diet quality and dietary patterns; intestinal microbiota, microbial translocation, and immunometabolism; interventions nutritional; food insecurity and immune activation; and metabolic syndrome, cardiovascular risk, and antiretroviral therapy. Table 1 presents the distribution of the studies according to the thematic axes identified.

Table 1 – Distribution of the included studies according to the thematic axis of the review

Thematic axis	Studies included	Main variables analyzed	Synthesis of the findings
Chronic inflammation, coagulation, and non–AIDS-defining events	1, 2, 3, 4	IL-6, CRP, usCRP, D-dimer, sCD14, sCD163, mortality, cardiovascular events, and non-AIDS events	Residual inflammation and coagulation activation persist even in treated individuals and are associated with mortality, cardiovascular risk, and non–AIDS-defining comorbidities
Diet quality and eating patterns	5, 6, 7, 8, 9, 10, 11, 12	Diet quality indices, Mediterranean diet pattern, Western diet pattern, fiber, fruits, vegetables, fats, dietary profile	People living with HIV often have inadequate dietary quality; healthier patterns have been associated with better metabolic profiles,

Theme axis	Studies included	Main variables analyzed	Synthesis of findings
			microbial and inflammatory
Intestinal microbiota, microbial translocation, and immunometabolism	9, 11, 12, 13, 14, 15, 26	Intestinal microbiome, metabolome, LPS, sCD14, I-FABP, dysbiosis, intestinal barrier, metabolic syndrome	Changes in the microbiota and the intestinal barrier may favor microbial translocation, persistent immune activation, and an increased metabolic risk
Nutrition interventions and inflammatory modulation	8, 9, 16, 17, 18, 19, 20, 21	Mediterranean diet, extra-virgin olive oil, omega 3, DHA, lipid profile, CRP, IL-6, TNF alpha, oxidative stress	Nutrition interventions can improve lipid, oxidative, and some inflammatory markers, although the effects are not uniform across all biomarkers
Food insecurity and immune activation	22, 23	Food insecurity, IL-6, TNFR1, sCD14, sCD27, sCD163, immune activation	Food insecurity was associated with higher inflammation and immune activation, indicating that nutritional vulnerability acts as a social determinant of inflammation in HIV
Metabolic syndrome, cardiovascular risk, and ART	3, 7, 14, 15, 24, 25	Dyslipidemia, insulin resistance, metabolic syndrome, microbiota, cardiovascular risk, antiretroviral regimens	The interaction between HIV, ART, inflammation, diet, and microbiota contributes to a higher burden of cardiometabolic changes

Classic studies on chronic inflammation in HIV have shown a consistent association between inflammatory biomarkers, coagulation, and adverse clinical outcomes. Deeks, Tracy, and Douek [1] highlighted that persistent systemic inflammation is one of the main mechanisms involved in premature aging and the development of comorbidities in people living with HIV. Kuller et al. [2] showed that IL-6 and D-dimer associated with an increased risk of mortality, while Duprez et al. [3] identified an association between inflammation, coagulation, and cardiovascular disease. Tenorio et al. [4], in turn, showed that soluble markers of inflammation and coagulation predict non-AIDS-defining morbid events during suppressive ART.

Regarding diet, studies have shown that the dietary quality of people living with HIV tends to be suboptimal. Weiss et al. [5] observed

low diet quality in this population, with differences according to sex and an association between better dietary quality and lower immune activation measured by sCD14. Duran et al. [6] also identified important dietary inadequacies in individuals under antiretroviral therapy, especially regarding the intake of fruits, vegetables, fiber, and dairy products. In a global cohort, Fitch et al. [7] showed that adults with HIV and traditional low to moderate cardiovascular risk still had dietary patterns that require preventive attention.

The findings related to dietary patterns indicated a possible benefit of diets with higher nutritional density and an anti-inflammatory profile. Stradling et al. [8] assessed a dietary intervention based on the Mediterranean/portfolio diet in people living with HIV and dyslipidemia, suggesting the potential applicability of the nutritional approach in managing cardiovascular risk. Pastor-Ibáñez et al.

[9] observed that adherence to a Mediterranean diet supplemented with these interventions was associated with favorable changes in the intestinal microbiota, improved metabolic parameters, immune activation, and the function of regulatory T cells. Manzano et al. [11] reinforced this relationship by demonstrating an association between diet, the intestinal microbiota, and inflammatory biomarkers in people living with HIV.

The analysis of the intestinal microbiota has emerged as a central axis of the findings. Multi-omics and observational studies indicated that dysbiosis, loss of intestinal barrier integrity, and microbial translocation may contribute to persistent immune activation and metabolic changes in people living with HIV [12-15,26]. Armstrong et al. [13] linked characteristics of the intestinal microbiome to metabolic and immunological phenotypes, while Baltazar-Díaz et al. [14] observed differences in intestinal bacterial communities in individuals with HIV and metabolic syndrome. MacCann et al. [15] added recent evidence on the association between the intestinal microbiome, inflammation, and cardiovascular profiles. Ouyang et al. [26] highlighted a relevance of biomarkers of intestinal injury and microbial translocation, such as LPS, sCD14, and I-FABP, in the persistence of systemic inflammation.

Intervention studies in nutrition showed promising results, although they were heterogeneous.

ISSN: **2764-4006** | www.revistacientificaipedss.com

Interventions with extra-virgin olive oil were evaluated in relation to inflammatory biomarkers, lipid profile, and intestinal microbiota [16, 17]. Supplementation with omega 3 was also investigated in clinical trials and systematic reviews, with findings indicating a possible reduction in C-reactive protein, but with no consistent effect on IL-6 and

TNF-alpha [18-21]. Domingo et al. [19] added the analysis of DHA on subcutaneous adipose tissue and inflammatory gene expression, highlighting the relevance of adipose tissue as an immunometabolic component in HIV.

Table 2 shows the main biomarkers and outcomes identified in the studies, as well as their interpretation within the relationship between HIV, nutrition, inflammation, and metabolic diseases.

Table 2 – Main biomarkers, nutritional variables, and outcomes analyzed in the included studies

Cat go ia	M d iá i	Study l io d	Int p t çã do h do
Systemic inflammation	IL-6, CRP, CRP-us, TNFa-lfa, TNFR1	2, 3, 4, 19, 20, 21, 22	Associated with persistent inflammation, mortality, cardiovascular risk, and variable response to nutritional interventions
Coagulation and cardiovascular risk	D-dimer, cardiovascular profile, events cardiovascular	2, 3, 4, 7, 15	The activation of coagulation appears as an important component of cardiovascular risk and non-AIDS morbidity
Immune and monocyte activation	sCD14, sCD163, sCD27	4, 5, 22, 23, 26	Markers associated with persistent immune activation, microbial translocation, and food insecurity
Intestinal barrier and microbial translocation	LPS, I-FABP, intestinal permeability, mucosal damage	10, 13, 26	Indicate a possible link between intestinal damage, the passage of microbial products, and systemic inflammation
Diet and food quality	Diet quality, Mediterranean diet pattern, Western diet pattern, fiber, fruit, vegetables, fats	5, 6, 7, 8, 9, 10, 11, 12	Higher-quality diets tend to be associated with a more favorable metabolic and inflammatory profile, although not all studies demonstrate a direct association
Microbiota and metabolome	Bacterial composition, microbial diversity,	9, 11, 12, 13, 14, 15	The gut microbiota appears as a potential mediator between diet,

Category	Markers or variables	Studies related	Interpretation of findings
	Fecal metabolome		inflammation and metabolic diseases
Nutrition interventions	Mediterranean diet, extra-virgin olive oil, omega 3, DHA	8, 9, 16, 17, 18, 19, 20, 21	Nutrition interventions can modulate lipid, oxidative, microbial, and inflammatory markers, with results depending on the type of intervention and the patient's profile
Metabolic diseases	Metabolic syndrome, dyslipidemia, insulin resistance, body changes	14, 15, 24, 25	The burden of metabolic changes is relevant in people living with HIV and results from the interaction between inflammation, ART, microbiota, and lifestyle
Social determinants of nutrition	Food insecurity, access to food, social vulnerability	22, 23	Food insecurity is associated with higher immune activation and inflammation, indicating that the social context interferes with clinical outcomes

Food insecurity was also identified as a relevant factor in the modulation of inflammation in people living with HIV. Leddy et al. [22] demonstrated an association between food insecurity and increased IL-6 and TNFR1 in women living with HIV. Tamargo et al. [23] observed that food insecurity was related to greater immune activation, expressed by markers such as sCD14, sCD27, and sCD163. These findings indicate that the nutritional status in HIV must be assessed beyond individual nutrient intake, including access nutritional, vulnerability socioeconomic status and living conditions.

Regarding metabolic diseases, the analyzed literature indicated that metabolic syndrome represents a condition of high clinical relevance in adults living with HIV. A meta-analysis by Trachuntthong et al. [24] showed a substantial global burden of metabolic syndrome in this population. Ergin et al. [25] discussed that HIV and ART can contribute to metabolic alterations such as dyslipidemia, insulin resistance, lipodystrophy, and

changes in body composition. These findings reinforce that the approach to metabolic comorbidities in people living with HIV must consider viral, immunological, pharmacological, nutritional, and behavioral factors.

Overall, the results indicate that the relationship between HIV, chronic inflammation, and nutrition is mediated by multiple interconnected pathways. Diet can influence systemic inflammation both directly, through the intake of nutrients, dietary patterns, and bioactive compounds, and indirectly, by modulating the intestinal microbiota, lipid metabolism, oxidative stress, the intestinal barrier, and immune activation. However, the findings also show that isolated nutritional interventions do not fully explain chronic inflammation in HIV, since this process involves viral, immunological, metabolic, social, and therapeutic factors.

Thus, the synthesis of the studies indicates that people living with HIV constitute a population at increased risk for persistent systemic inflammation and metabolic diseases, even in the era of effective antiretroviral therapy. The quality of the diet, the Food insecurity, the intestinal microbiota, and specific nutritional interventions should be considered relevant components in clinical care and cardiometabolic prevention for this population. These findings support the need for integrated strategies that combine virological control, nutritional follow-up, metabolic assessment, monitoring of inflammatory biomarkers, and the promotion of healthy eating patterns.

DISCUSSION

The findings of this integrative review with a systematized approach show that the relationship between HIV, chronic inflammation, and nutrition is complex and multidimensional and strongly influenced by the interaction among immunological, metabolic, intestinal, dietary, therapeutic, and social factors. Although antiretroviral therapy has profoundly modified the clinical course of HIV infection—reducing AIDS-associated mortality and increasing life expectancy—the analyzed literature indicates that viral suppression does not completely eliminate persistent immune activation or the increased risk of chronic comorbidities [1-4]. This aspect is central to

understand why people living with HIV have greater vulnerability to diseases cardiovascular disease, metabolic syndrome, liver changes, dyslipidemia, insulin resistance, and other non-AIDS-defining outcomes [3,24,25].

Residual systemic inflammation appears as an essential pathophysiological axis in this population. Classic studies showed that markers such as IL-6, D-dimer, high-sensitivity CRP, sCD14, and sCD163 are associated with mortality, cardiovascular events, and non-AIDS-defining morbidities [2-4]. These findings indicate that the clinical assessment of people living with HIV should not be limited to monitoring viral load and CD4+ T-cell counts, since the risk of chronic illness may persist even in individuals with a good virological response to ART. In this sense, chronic inflammation in HIV should be interpreted as an immunometabolic underlying phenomenon, in which sustained inflammatory responses contribute to endothelial alterations, coagulation, adipocyte dysfunction, intestinal dysbiosis, and increased susceptibility to chronic diseases [1,3,4].

One of the main points identified in this review is the role of diet as a possible modulator of inflammation and metabolic risk in people living with HIV. Studies on dietary quality have shown that this population frequently has inadequate dietary patterns, with low intake of fruits, vegetables, fiber, and foods with higher nutritional density [5-7]. Such inadequacies may contribute to a worse lipid profile, greater adiposity, changes in the gut microbiota, and the intensification of inflammatory pathways. The low diet quality observed in studies such as those by Weiss et al. [5] and Duran et al. [6] reinforces the need to include nutritional assessment as part of longitudinal care in HIV, especially in patients with cardiovascular risk, metabolic syndrome, or laboratory signs of persistent inflammation.

Despite this, the relationship between diet and inflammation in HIV should not be interpreted in a linear way. Malazogu et al. [10], for example, did not identify a significant association between the Dietary Inflammatory Index, intestinal permeability, and systemic inflammation biomarkers in people with HIV who were immunologically non-responders. This finding is relevant because it shows that the

Chronic inflammation in HIV cannot be attributed exclusively to diet. In many cases, factors such as prior mucosal damage, persistent microbial translocation, a history of immunosuppression, duration of infection, the composition of ART, coinfections, age, adiposity, and social factors can modulate the inflammatory response independently of the dietary pattern assessed [1,4, 10,26]. Thus, nutrition should be understood as an important component, but not isolated, within a broader causal network.

Among the dietary patterns investigated, the Mediterranean diet stands out as one of the most promising approaches. Studies included in this review suggest that dietary patterns rich in minimally processed foods, fiber, unsaturated fats, fruits, vegetables, legumes, and olive oil may support a better metabolic profile, a healthier intestinal composition, and a possible reduction in inflammatory markers [8,9, 11]. Pastor-Ibáñez et al. [9] showed that adherence to a Mediterranean diet supplemented with these components was associated with changes in the gut microbiota, improved metabolic parameters, immune activation, and the function of regulatory T cells in infected individuals by HIV-1. These findings suggest that nutritional intervention may affect not only traditional metabolic markers, but also immunological and microbial mechanisms related to chronic inflammation.

The gut microbiota appears as a fundamental interface between diet, HIV, inflammation, and metabolic diseases. The literature analyzed indicates that the gastrointestinal tract is a critically affected compartment in HIV infection, with damage to the mucosal barrier, changes in local immunity, and increased translocation of microbial products into systemic circulation [1,26]. This process may stimulate monocytes and macrophages, increase the expression of markers such as sCD14 and sCD163, and contribute to maintaining systemic immune activation [4, 13,26]. Thus, intestinal dysbiosis represents not only a local alteration, but a possible systemic mechanism for perpetuating inflammation and metabolic risk.

Multi-omics and observational studies reinforce this interpretation by showing an association between the gut microbiome, fecal metabolome, liver health, metabolic syndrome, and profiles

cardiovascular in people living with HIV [12-15]. Armstrong et al. [13] demonstrated that the intestinal microbiome can influence metabolic and immunological phenotypes in HIV-positive and high-risk populations. Baltazar-Díaz et al. [14] observed differences in intestinal bacterial communities in individuals with HIV and metabolic syndrome, while MacCann et al. [15] linked the intestinal microbiota, inflammation, and cardiovascular profiles. These findings support the hypothesis that part of the cardiometabolic risk in HIV may be mediated by the gut, immunity, and metabolism axis.

The nutritional interventions evaluated in the included studies showed relevant results, but were still heterogeneous. Extra-virgin olive oil was investigated in relation to inflammatory biomarkers, the lipid profile, and the intestinal microbiota, with potential benefit in parameters related to atherosclerosis and lipid metabolism [16,17]. Supplementation with omega 3 also proved promising, especially due to the possibility of reducing C-reactive protein and modulating oxidative stress, although the effects on IL-6, TNF-alpha and other inflammatory markers not have been consistent across all studies [18-21]. This heterogeneity suggests that isolated nutritional interventions may show specific benefits, but they probably depend on the dose, duration, the composition of the usual diet, baseline inflammatory status, the presence of dyslipidemia, the type of cART, and the patient**,** s metabolic profile.

Another important aspect is the role of adipose tissue as an immunometabolic organ. Domingo et al. [19] evaluated the effect of DHA on inflammatory markers and gene expression in subcutaneous adipose tissue in patients with HIV on combined antiretroviral therapy. This type of evidence broadens the understanding of metabolic inflammation in HIV, because it shows that body changes, visceral fat accumulation, adipocyte dysfunction, and lipodystrophy may contribute to the production of inflammatory mediators and to an increased cardiometabolic risk. Therefore, the nutritional approach should consider not only circulating biomarkers, but also body composition, fat distribution, insulin resistance, and overall metabolic health [19,25].

Food insecurity deserves special attention for representing a

the social dimension often neglected in discussions about inflammation and nutrition in HIV. Studies by Leddy et al. [22] and Tamargo et al. [23] showed an association between food insecurity and elevated inflammatory markers and immune activation, including IL-6, TNFR1, sCD14, sCD27, and sCD163. These findings indicate that inflammatory risk is not determined only by individual food choices, but also by the concrete conditions for access to adequate food, economic stability, social vulnerability, and the ability to maintain a healthy diet. Therefore, nutritional strategies for people living with HIV should incorporate food security policies, nutrition education, access to quality food, and multidisciplinary follow-up.

metabolic syndrome and cardiovascular risk represent key clinical outcomes in this discussion. The meta-analysis by Trachunthong et al. [24] showed a substantial burden of metabolic syndrome in the adult population living with HIV, reinforcing that metabolic changes are a global issue in this population. Such changes can be explained by the combination of chronic inflammation and adverse effects of certain antiretrovirals, aging, sedentary lifestyle, inadequate diet, changes in the microbiota, and individual predisposition [24,25]. Therefore, HIV should be understood as a chronic condition that requires permanent metabolic monitoring, especially in individuals with long exposure to ART or with additional cardiovascular risk factors.

From a clinical point of view, the results of this review suggest that nutritional care in people living with HIV should take on a preventive, therapeutic, and individualized nature. Dietary assessment should consider the overall quality of the diet, fiber intake, fruits, vegetables, saturated fats, unsaturated fats, ultra-processed foods, alcohol consumption, the predominant dietary pattern, and the presence of food insecurity. In addition, nutritional management should be integrated with laboratory assessment of the lipid profile, blood glucose, insulin resistance, body composition, hepatic markers, and, when possible, inflammatory biomarkers. This integrated approach can help reduce cardiometabolic risk and improve the quality of life of this population.

However, it is necessary to recognize important limitations of the analyzed literature. Many studies use a cross-sectional design, which limits causal inferences between diet, inflammation, and metabolic outcomes. In addition, there is heterogeneity regarding the dietary assessment instruments, inflammatory markers analyzed, participants' clinical characteristics, infection duration, antiretroviral regimens, and criteria for defining metabolic syndrome. There is also a lack of clinical trials

of larger scale and longer duration evaluating comprehensive dietary interventions in people living with HIV. These aspects make it difficult to develop specific and universal recommendations about nutritional interventions for modulating inflammation in this population.

Even so, the available studies make it possible to state that nutrition plays a strategic role in the care of people living with HIV. Diet can influence inflammatory pathways, the intestinal microbiota, lipid metabolism, oxidative stress, body composition, and cardiovascular risk [5,8,9, 11, 16-21]. However, the impact of nutrition depends on individual and contextual factors, including adherence to ART, immune status, social vulnerability, food security, microbiota pattern, presence of comorbidities, and metabolic profile. Thus, nutritional management in HIV must be understood as part of an interdisciplinary approach, involving infectious disease medicine, nutrition, cardiology, endocrinology, public health, and psychosocial care.

In summary, the discussion of the included studies shows that chronic inflammation in HIV remains a relevant clinical challenge in the era of ART. Diet, the gut microbiota, and nutritional conditions play an important role in modulating this process, but they do not act in isolation. The interaction between residual inflammation, microbial translocation, metabolic changes, food insecurity, and inadequate dietary patterns contributes to increasing the risk of metabolic and cardiovascular diseases. Therefore, nutritional interventions based on healthy dietary patterns, combined with metabolic monitoring and addressing food insecurity, represent promising pathways to reduce the burden of chronic morbidities in people living with HIV.

CONCLUSION

This integrative review with a systematized approach showed that the relationship between HIV, chronic inflammation, and nutrition involves multiple interdependent mechanisms, including persistent immune activation, changes in the intestinal barrier, microbial translocation, dysbiosis, metabolic alterations, effects of antiretroviral therapy, diet quality, and food-safety conditions. Even in the era of effective antiretroviral therapy, people living with HIV may present residual systemic inflammation associated with an increased risk of non-AIDS-defining morbidities, cardiovascular diseases, metabolic syndrome, dyslipidemia, insulin resistance, and changes in body composition.

The analyzed studies demonstrated that biomarkers such as IL-6, C-reactive protein, D-dimer, sCD14, sCD163, TNF-alpha, TNFR1, LPS, and I-FABP are relevant for understanding the persistence of inflammation and its association with clinical and metabolic outcomes. These markers indicate that monitoring people living with HIV should go beyond viral load and the count of CD4+ T lymphocytes, by incorporating cardiometabolic assessment, nutritional, inflammatory, and, when possible, intestinal.

The quality of the diet proved to be an important component in modulating metabolic and inflammatory risk. Inadequate dietary patterns, characterized by low intake of fruits, vegetables, fiber, and foods with higher nutritional density, may contribute to a worse cardiometabolic profile and greater inflammatory vulnerability. On the other hand, healthier dietary patterns, especially those close to the Mediterranean diet, were associated with a better metabolic profile, a more favorable gut microbiota, and a possible reduction in inflammatory markers in certain groups.

The nutritional interventions evaluated, including the Mediterranean diet, extra-virgin olive oil, omega-3 and DHA, showed promising results, especially regarding lipid profile, oxidative stress, C-reactive protein, gut microbiota, and metabolic parameters. However, the effects were not uniform for all inflammatory markers, such as IL-6 and TNF-alpha, demonstrating that nutrition should be understood as a complementary and integrated strategy, and not as a

an isolated intervention capable of eliminating the chronic inflammation associated with HIV.

Another relevant finding was the importance of food insecurity as a social determinant of inflammation. Difficulty in obtaining regular access to adequate food showed an association with greater immune activation and elevated inflammatory markers, indicating that nutritional care for people living with HIV should consider not only individual food choices, but also social, economic, and structural vulnerabilities.

It is concluded that nutrition plays a strategic role in comprehensive care for people living with HIV, especially in the prevention and management of metabolic and cardiovascular diseases. Integration between viral control, nutritional assessment, promotion of healthy eating patterns, monitoring metabolic, tracking body composition, and addressing food insecurity can help reduce the inflammatory burden and improve clinical outcomes in this population.

Despite the advances, there are still needed longitudinal studies and larger randomized clinical trials in order to clarify the causality between Diet, microbiota, inflammation, and metabolic diseases in HIV, as well as defining more specific, individualized, and sustainable nutritional interventions. Future research should consider the diversity of antiretroviral regimens, patients' immunological profile, the pattern of intestinal microbiota, the presence of comorbidities, and the social determinants of food.

REFERENCES

1. Deeks SG, Tracy R, Douek DC. Systemic effects of inflammation on health during chronic HIV infection. *Immunity*. 2013;39(4):633-645. doi: 10. 1016/j.immuni.2013.10.001. A central study on persistent systemic inflammation in HIV and the risk of cardiovascular, hepatic, renal, bone, and neurological comorbidities.

2. Kuller LH, Tracy R, Belloso W, De Wit S, Drummond F, Lane HC, et al. Inflammatory and coagulation biomarkers and mortality in patients with HIV infection. *PLoS Med*. 2008;5(10):e203. doi:10. 1371/journal.pmed.0050203. A classic study demonstrating an association between inflammatory/coagulation biomarkers, especially IL-6 and D-dimer, and mortality in people with HIV.

3. Duprez DA, Neuhaus J, Kuller LH, Tracy R, Belloso W, De Wit S, et al. Inflammation, coagulation and

cardiovascular disease in HIV infected individuals. *PLoS One*. 2012;7(9):e44454. doi:10.1371/journal.pone.0044454.

Baseline strength to discuss IL-6, high-sensitivity CRP, and D-dimer as markers associated with cardiovascular risk in HIV.

4. Tenorio AR, Zheng Y, Bosch RJ, Krishnan S, Rodriguez B, Hunt PW, et al. Soluble markers of inflammation and coagulation but not T-cell activation predict non-AIDS-defining morbid events during suppressive antiretroviral treatment.*JInfect Dis*. 2014;210(8):1248-1259. doi:10.1093/infdis/jiu254. Essential to show that non–AIDS-defining events persist even with suppressive ART and are related to inflammation/coagulation.

5. Weiss JJ, Sanchez L, Hubbard J, Lo J, Grinspoon SK, Fitch KV. Diet quality is low and differs by sex in people with HIV. *J Nutr*. 2019;149(1):78-87. doi:10.1093/jn/nxy241.

Study directly related to diet quality in people living with HIV and its association with immunoinflammatory markers.

6. Duran ACFL, Almeida LB, Segurado AAC, Jaime PC. Diet quality of persons living with HIV/AIDS on highly active antiretroviral therapy. *J Hum Nutr Diet*. 2008;21(4):346-350. doi:10.1111/j.1365-277X.2008.00886.x.

Relevant Brazilian study to discuss dietary inadequacies in adults living with HIV/AIDS on antiretroviral therapy.

7. Fitch KV, McCallum SA, Erlandson KM, Overton ET, Zanni MV, Fichtenbaum CJ, et al. Diet in a global cohort of adults with HIV at low-to-moderate traditional cardiovascular disease risk. *AIDS*. 2022;36(14):1997-2003.

REPRIEVE cohort study, useful to support that diet quality is often suboptimal in adults with HIV eligible for primary cardiovascular prevention.

8. Stradling C, Thomas GN, Hemming K, Taylor S, Teo KW, Back D, et al. Randomized parallel-group pilot trial (Best foods for your heart) comparing the effects of a Mediterranean Portfolio diet with a low saturated fat diet on HIV dyslipidemia.*Clin Nutr*.

2021. Relevant pilot trial about Mediterranean/portfolio diet in people living with HIV and dyslipidemia.

9. Pastor-Ibáñez R, Blanco-Heredia J, Etcheverry F, Sánchez-Palomino S, Díez-Fuertes F, Casas R, et al. Adherence to a supplemented Mediterranean diet drives changes in the gut microbiota of HIV-1-infected individuals. *Nutrients*. 2021;13(4):1141. doi:10.3390/nu13041141.

Fundamental study to integrate the Mediterranean diet, gut microbiota, metabolic parameters, and immune activation in HIV.

10. Malazogu F, Rousseau RK, Shivappa N, Huibner S, Walmsley SL, Kovacs CM, et al. The Dietary Inflammatory Index is not associated with gut permeability or biomarkers of systemic inflammation in HIV

immunologic non-responders. *Front Nutr*. 2021;8:736816. doi:10.3389/fnut.2021.736816.

Important for bringing a negative result, showing that not always the inflammatory index of the diet explains inflammation systemic in immunologic non-responders.

11. Manzano M, Talavera-Rodríguez A, Moreno E, Madrid N, Gosalbes MJ, Ron R, et al. Relationship of diet to gut microbiota and inflammatory biomarkers in people with HIV. *Nutrients*. 2022;14(6):1221. doi:10.3390/nu14061221.

Highly relevant to the topic, as it assesses diet, the intestinal microbiota, and inflammatory biomarkers in people with HIV.

12. Martin HR, Martinez SS, Stebliankin V, et al. Diet quality and liver health in people living with HIV in the MASH cohort: a multi-omic analysis of the fecal microbiome and metabolome. *Metabolites*. 2023;13(2):271. doi:10.3390/metabo13020271.

Important foundation for discussing diet, the fecal microbiome, the metabolome, and the gut—liver axis in people living with HIV.

13. Armstrong AJS, Shaffer M, Nusbacher NM, Griesmer C, Fiorillo S, Schneider JM, et al. Systems analysis of gut microbiome influence on metabolic disease in HIV-positive and high-risk populations. *mSystems*. 2021.

A relevant multi-omic study for linking the gut microbiome, immune markers, and translocation bacteria and metabolic health in HIV.

14. Baltazar-Díaz TA, Amador-Lara F, Andrade-Villanueva JF, GonzálezHernández LA, Cabrera-Silva RI, Sánchez-Reyes K, et al. Gut bacterial communities in HIV-infected individuals with metabolic syndrome: effects of therapy with integrase strand transfer inhibitor-based and protease inhibitor-based regimens.*Microorganisms*. 2023;11(4):951. doi:10.3390/microorganisms1104095 1.

Relevant for discussing metabolic syndrome, the intestinal microbiota, and potential differences associated with antiretroviral regimens.

15. MacCann R, et al. Associations between the gut microbiome, inflammation, and cardiovascular profiles in people with human immunodeficiency virus. *J Infect Dis*. 2025;231(4):e781-e791.

Study recent connecting gut microbiota, diet, inflammation, and cardiovascular profiles in people living with HIV.

16. Dokmanović SK, Kolovrat K, La§kaj R, Jukić V, Vrkić N, Begovac J. Effect of extra virgin olive oil on biomarkers of inflammation in HIV-infected patients: a randomized, crossover, controlled clinical trial.*Med Sci Monit*. 2015;21:2406-2413. Clinical trial on extra virgin olive oil and inflammatory/atherosclerotic biomarkers in HIV patients.

17. Olalla J, García de Lomas JM, Chueca N, Pérez-Stachowski X, De

Salazar A, Del Arco A, et al. Effect of daily consumption of extra virgin olive oil on the lipid profile and microbiota of HIV-infected patients over 50 years of age. *Medicine*. 2019;98(42):e17528.
doi:10. 1097/MD.0000000000017528.

Useful study to discuss nutritional intervention with olive oil, lipid profile, and microbiota diversity in patients with HIV over 50 years of age.

18. Amador-Licona N, Díaz-Murillo TA, Gabriel-Ortiz G, Pacheco-Moisés FP, Pereyra-Nobara TA, Guízar-Mendoza JM, et al. Omega 3 fatty acids supplementation and oxidative stress in HIV-seropositive patients: a clinical trial. *PLoS One*. 2016;11(3):e0151637.
doi:10. 1371/journal.pone.0151637.
Clinical trial on omega-3 supplementation and oxidative stress in HIV-positive patients.

19. Domingo P, Gallego-Escuredo JM, Fernández I, Villarroya J, Torres F, Gutiérrez MM, et al. Effects of docosahexanoic acid supplementation on inflammatory and subcutaneous adipose tissue gene expression in HIV-infected patients on combination antiretroviral therapy: a sub-study of a randomized, doublebli nd, placebo-controlled study.*Cytokine*. 2018;105:73-79.
doi:10. 1016/j.cyto.2018.02.008.
Important study to discuss DHA, triglycerides, high-sensitivity CRP, and inflammatory gene expression in adipose tissue.

20. Morvaridzadeh M, Agah S, Nachvak SM, Fazelian S, Moradi F, Heshmati J. The effects of omega-3 fatty acid supplementation on inflammatory factors in HIV-infected patients: a systematic review and meta-analysis of randomized clinical trials. *Cytokine*. 2020.
A relevant meta-analysis indicates that omega-3 reduces CRP in HIV patients, with no consistent effect on IL-6 and TNF-alpha.

21. Bai J, Cao Y, Wang L, Ni J, Zhu Y, Wei T. Effect of omega-3 supplementation on metabolic and inflammatory markers in adults with HIV infection: a systematic review and meta-analysis.*Front Nutr*. 2026.
Very recent study, useful for updating the discussion on omega-3, markers metabolic and inflammatory in adults with HIV.

22. Leddy AM, Roque A, Sheira LA, Frongillo EA, Landay AL, Adedimeji AA, et al. Food insecurity is associated with inflammation among women living with HIV. *J Infect Dis*. 2019;219(3):429 -436. doi:10. 1093/infdis/jiy511.
An essential study to discuss food insecurity as a factor associated with inflammation in women living with HIV.

23. Tamargo JA, Hernandez-Boyer J, Teeman C, et al. Immune activation: a link between food insecurity and chronic disease in people living with human immunodeficiency virus. *J Infect Dis*. 2021;224(12):2043 -2052.doi:10. 1093/infdis/jiab257.
Relevant basis for connecting food insecurity, immune activation, sCD14, sCD27, sCD163, and the risk of chronic diseases in HIV.

24. Trachunthong D, Tipayamongkholgul M, Chumseng S, Darasawang W, Bundhamcharoen K.Burden of metabolic syndrome in the global adult HIV-infected population: a systematic review and meta analysis. *BMC Public Health*. 2024;24:2657. doi:10.1186/s12889-024-20118-3.
Global meta-analysis essential to underpin the burden of metabolic syndrome among adults living with HIV.

25. Ergin HE, Inga EE, Maung TZ, Javed M, Khan S. HIV, antiretroviral therapy and metabolic alterations: a review. *Cureus*. 2020;12(5):e8059. doi:10.7759/cureus.8059.
Useful review for contextualizing metabolic alterations associated with HIV and antiretroviral therapy, including dyslipidemia, resistance to insulin, and body changes.

26. Ouyang J, Isnard S, Lin J, Fombuena B, Peng X, Routy JP, et al. Relevance of biomarkers indicating gut damage and microbial translocation in people living with HIV.*Front Immunol*. 2023. Important critical review to support intestinal permeability, microbial translocation, LPS, sCD14, I-FABP, and immune activation in HIV.