

Evaluation of HDL/Monocyte Ratio as a Predictor of Cardiovascular Diseases in People Living with HIV

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ABSTRACT

This study investigated the correlation between absolute monocyte count and HDL levels, aiming to understand their role as a risk indicator for cardiovascular diseases (CVD) in people living with HIV (PLHIV). The research involved a search for scientific articles in the PubMed and EBSCO databases using the PICOT strategy (Population, Intervention, Comparison, Outcome, and Time), along with a table summarizing key information from selected articles based on specific criteria. This was followed by a detailed discussion correlating the findings. Results indicated that the HDL/Monocyte ratio has potential as a CVD marker due to its association with the pathogenesis of atherosclerosis, despite limited studies validating its use in PLHIV. The observed correlation between HDL levels and inflammatory markers, especially MCP-1, reinforces its promising potential for future investigations. This is supported by its potential for clinical management, given that it is a simple, cost-effective method. However, further targeted studies are necessary to investigate the applicability and sensitivity of this marker in PLHIV. The study also proposed exploring complementary strategies to antiretroviral therapy (ART) for controlling chronic inflammation from HIV infection, preventing other related diseases in PLHIV.

Keywords: Good Health and Well Being; HIV; Cardiovascular Disease; HDL; Monocyte

INTRODUCTION

Human immunodeficiency virus (HIV) infection remains one of the greatest global public health crises. Since the beginning of the epidemic in the 1980s, approximately 42.3 million people have died due to complications related to the virus. Despite significant advances in prevention, treatment, and disease control, the World Health Organization (WHO) reports that more than 38 million people are currently living with HIV (PLHIV). Transmission of the virus still occurs in virtually every country in the world, with millions of new cases reported annually. In Brazil, 541,759 cases of HIV infection were reported between 2007 and June 2024, with the regional distribution as follows: Southeast: 222,262 cases (41.0%); Northeast: 118,431 (21.9%); South: 101,441 (18.7%); North: 56,229 (10.4%); and Central-West: 43,396 (8.0%). Without appropriate treatment, HIV infection can progress to acquired immunodeficiency syndrome (AIDS), the most advanced stage of the disease, characterized by severe immunosuppression and the emergence of opportunistic infections and cancers [1]. To ensure the benefits of immediate initiation of antiretroviral therapy (ART), early diagnosis of HIV infection is crucial. Although testing strategies exist, many cases are still diagnosed at advanced stages. According to the 2024 clinical protocol and therapeutic guidelines for managing HIV infection in adults, after diagnosis, it is essential to adopt an initial approach based on welcoming the patient, including assessing medical history, physical examination, and complementary tests to determine infection stage, possible coinfections, or comorbidities. Additionally, understanding the patient's life context and vulnerabilities and establishing a relationship of trust and respect with health professionals are fundamental for therapeutic success and comprehensive care.

Initial HIV infection treatment should include three antiretroviral medications: two nucleoside/nucleotide reverse transcriptase

inhibitors (NRTIs) and a third from another class, such as an integrase inhibitor (INI), protease inhibitor with ritonavir (PI/r), or a non-nucleoside reverse transcriptase inhibitor (NNRTI). The preferred regimen for treatment initiation consists of a combination of tenofovir, lamivudine, and dolutegravir, administered as a once-daily fixed-dose combination, available through the Brazilian public health system (SUS). ART should be started on the same day or within seven days of diagnosis and is highly effective for preventing HIV transmission, controlling viral replication and disease progression to AIDS, as well as improving patient quality of life. With treatment adherence, PLHIV can achieve and maintain an undetectable viral load, eliminating the risk of sexual transmission and significantly extending life expectancy. Thus, HIV, once considered a death sentence, has become a chronic condition allowing patients to live healthy and long lives comparable to those without the virus. As PLHIV age, the risk of developing age-related chronic diseases increases significantly, including frailty, metabolic, neurodegenerative, and cardiovascular disorders, even in patients with adequate virological control [2]. This increase in morbidity is influenced by chronic inflammation, immune dysfunction, coinfections, behavioral factors, and continuous use of antiretrovirals, which may cause cumulative toxic effects and organ damage, limiting long-term benefits [3]. Cardiovascular disease (CVD) is the leading cause of mortality in Brazil and worldwide, with increasing cases driven by population aging. These include ischemic coronary artery disease (chronic angina and myocardial infarction), cerebrovascular disease (stroke and transient ischemic attack), other heart diseases (including arrhythmias, inflammatory heart disease, valvular disease, rheumatic heart disease, and heart failure), and other cardiovascular diseases (peripheral vascular disease, aortic aneurysms, and hypertensive disease) [4]. Classic risk factors such as

hypertension, dyslipidemia, obesity, physical inactivity, smoking, diabetes, and family history are determinants in primary and secondary prevention of CVD, especially coronary artery disease (CAD). Very high cardiovascular risk patients include those with significant atherosclerosis, elevated LDL cholesterol levels, diabetes with target organ damage, and chronic kidney disease. Monitoring these factors guides interventions to reduce cardiovascular risk [5]. Specifically, the risk of CVD in PLHIV is 2.16 times higher than in individuals without HIV[6]. Although ART reduces CVD risk, some drugs such as abacavir and protease inhibitors have been linked to increased risk, generating debate about ART's role in these complications [7]. In recent years, new cardiovascular risk markers have been identified to facilitate detection in the circulatory system, leading to more precise diagnosis. These include C-reactive protein (CRP), glomerular filtration rate (GFR), microalbuminuria, cystatin C, homocysteine, cytokines, cardiac troponins, and exosomes[8, 9]. However, in PLHIV, it is important to note that common CVD risk factors are insufficient to accurately predict CVD risk in this specific population. This is due to persistent chronic inflammation and immune activation, even in individuals under antiretroviral therapy (ART) with effective virological control [10]. Chronic inflammation caused by HIV maintains a constant state of immune activation, directly impacting the cardiovascular system. Monocytes, key immune cells involved in atherosclerotic plaque formation, play a fundamental role in this process [11]. In PLHIV, increased monocyte activation and elevated inflammatory biomarkers such as soluble CD163 and CD14 are associated with atherosclerotic plaque development. Additionally, HIV infection enhances foam cell formation in arteries, worsening the inflammatory process and promoting CVD development[4]. Another relevant aspect is the impact of HIV on cholesterol levels, especially HDL. In PLHIV, HDL tends to be oxidized (oxHDL), reducing its protective capacity against atherosclerosis. HDL oxidation is associated with systemic inflammation and increased markers such as interleukin-6 (IL-6) and high-sensitivity C-reactive protein (hs-CRP) [4]. The combination of reduced HDL function and increased

monocyte activation creates an environment highly prone to CVD development [11]. In this context, the HDL/monocyte ratio emerges as a promising tool to assess CVD risk in PLHIV. The ratio between HDL and monocyte count may reflect the body's capacity to protect itself against inflammation and atherosclerotic plaque formation, allowing a more precise cardiovascular risk assessment in PLHIV. It offers a broader view of the complex interaction among chronic inflammation, immune activation, and lipid dysfunction in this scenario, contributing to the evaluation and management of cardiovascular disease risk in this population.

Methods

The article search was conducted in the PubMed and EBSCO databases after formulating key questions using the PICOT criteria and employing standardized descriptors from the DeCS/MeSH vocabulary: "HIV," "Monocyte," and "HDL Cholesterol." Inclusion filters were applied to select only articles published between 2005 and 2024, written in English, and available in full text (Chart 1 – PRISMA flowchart). From this, 29 articles were identified—16 in the PubMed database and 13 in EBSCO. Of these, 11 were excluded due to duplication, and 2 other articles were discarded for not being available in full text, leaving 16 articles. At this stage, the abstracts of the remaining articles were read to ensure they were directly related to the study topic. After this screening, 5 articles were excluded for not meeting the specific research criteria, meaning they were outside the scope of the work, resulting in 11 articles selected for full reading and detailed analysis. Nine articles were considered for the review, as during the course of the work, 2 articles were excluded because they were not available in full text (Figure 1, 1-3). The analysis of the selected studies was conducted to identify and establish evidence of the relationship between monocytes and HDL levels as predictors of cardiovascular risk in people living with HIV (PLHIV). The presented data are organized in Chart 1 to allow comparisons among studies, highlighting the quantity and scope of relevant data for the proposed relationship analysis.

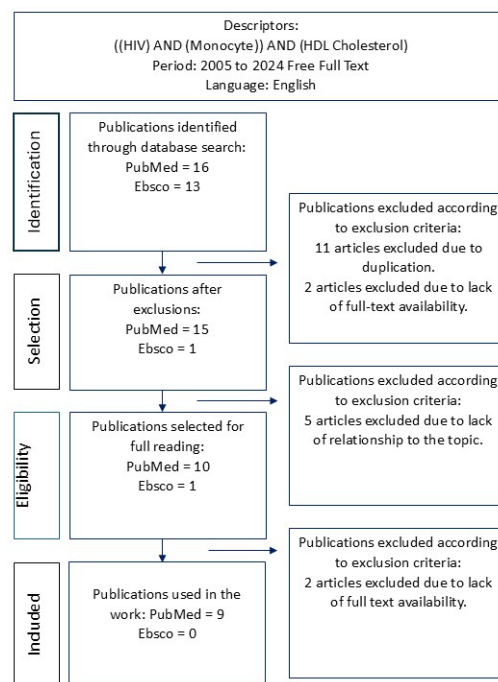


CHART 1: Flowchart. (Source: Prisma Software, by Author.)

Results

Publication Data	Type of Study	Aims of the Setudy	Methods and Results	Conclusions
Tribble ET, AL 2017 The Journal of Clinical Endocrinology & Metabolism, Volume 102	Prospective study	To evaluate cholesterol efflux capacity (HCEC) in the context of ART initiation and immune activation in HIV.	The methodology consisted of a comparison between a group of 10 HIV-infected men without previous treatment and another group of 12 HIV-infected men. Cholesterol efflux capacity was measured by transferring cholesterol from murine macrophages to HDL particles under varying conditions, including the use of apolipoprotein B (apoB)-depleted serum and purified HDL from the participants. As a result, it was found that HCEC levels were significantly lower in PLHIV than in the HIV-free group, and that, after 6 months of ART (raltegravir/abacavir/emtricitabine/tenofovir), HCEC increased in PLHIV, but did not reach the levels of HIV-free controls. There was also an inverse relationship between the increase in HCEC and the decrease in CD14- and CD16+ monocytes, and a direct relationship with the increase in CD14- and CD16- monocytes.	he article highlights the importance of monocyte counts especially the increase in classical monocytes and the reduction in non-classical monocytes, which appear to reflect improvements in HDL function in PLHIV after initiation of ART. The persistent changes in the monocyte profiles suggest that chronic inflammation may continue to affect HDL function, increasing cardiovascular risk in PLHIV even after initiation of ART.
Zunguopijom et. AL, 2016 PLoS ONE 11(2)	Cohort study	To examine the correlation between non-classical monocytes, MCP-1 protein (soluble chemokine regulator of inflammation, CAC measurements were obtained using monocytes) and progression of coronary artery calcium (CAC) in PLHIV (Adults) on stable ART.	This longitudinal analysis was performed using baseline and follow-up data from 78 participants with chronic HIV infection, for a period of 2 years, where analyses of monocyte subpopulations by flow cytometry in peripheral blood and biomarkers were performed. Soluble markers of inflammation, CAC measurements were obtained by computed tomography using the Agatston score. Arterial calcification was measured based on CAC values at baseline and at the end of the study (after 2 years). A positive correlation with CAC progression was observed between the percentage of non-classical monocytes and MCP-1 levels at 2 years, even after adjusting for traditional risk factors using Spearman's correlation.	A higher baseline percentage of non-classical monocytes and MCP-1 levels were found to be possibly associated with greater CAC progression within 2 years, thus suggesting that the high risk of CVD in PLHIV on ART may be related to immune activation and monocyte recruitment into atherosclerotic plaques
Mukhamedova et. AL, 2019 Atherosclerosis, Volume 265, Is sue 2, 439- 443	Experimental study	To evaluate the effect of various classes of antiretroviral drugs for the treatment of HIV on cellular cholesterol efflux	Seven antiretroviral drugs widely used for HIV treatment were analyzed to observe their effects on cholesterol efflux in murine macrophage cells (RAW264.7) and in macrophages derived from HDL and apolipoprotein A-I (apoA-I), in addition to evaluating the cytotoxicity of the compounds at pharmacological concentrations. It was observed that the antiretroviral drugs Neftravir and Ritonavir inhibited cholesterol efflux from macrophages to apoA-I only at high concentrations, causing significant cell apoptosis, linking the effects to the cytotoxicity of these drugs.	The article confirms that macrophage cholesterol efflux is not affected by the seven antiretrovirals tested at non-cytotoxic concentrations. Even Ritonavir and nevirapine did not directly impact cholesterol efflux at therapeutic concentrations, with the effect on efflux being linked to the toxicity of these drugs at high concentrations. Antiretrovirals appear to contribute to the increased risk of atherosclerosis in PLHIV by increasing direct cholesterol transport. Meanwhile, the infection itself appears to be responsible for compromising reverse cholesterol transport, overloading the cells and potentially transforming them into foam cells, which can directly contribute to the increased risk of atherosclerotic plaque formation.

FIGURE 1-1: Review of the selected articles.

Publication Data	Type of Study	Aims of the Setudy	Methods and Results	Conclusions
DiYacovo, et. AL, 2020 PLoS One, 2020;15(8):e0237729.	Prospective study	Investigation of the effect of HIV infection and ART on lipids and proatherogenic biomarkers and the relationship of these effects with subclinical atherosclerosis in treatment-naïve PLHIV	The study comprised 84 participants divided into three groups: group A, consisting of HIV-positive patients with CD4 counts >500 cells/μL who had not yet initiated ART; group B, consisting of patients with CD4 counts <500 cells/μL who had initiated ART at the initial visit; and the HIV-positive control group. Clinical, laboratory, and carotid ultrasound evaluations were performed on the participants for 2 years to correlate changes in LDL phenotype, inflammation, and infection biomarker levels with subclinical atherosclerosis. The levels of inflammatory and immunological activation markers showed an increase, and the lipid profile showed an unfavorable result in patients without ART compared to the control group, with the start of ART being related to the improvement of this scenario, reaching results very close to the control group, with the exception of hs-CRP, which remained higher, suggesting that higher levels of sCD163, sCD14 and hs-CRP may be associated with lower levels of total cholesterol (TC) and HDL-c and higher levels of TG/HDL and triglycerides.	According to the study, ART contributes to an improvement in the lipid profile, biomarkers of immune activation, and the LDL phenotype. However, it was recorded that, even with ART, carotid IMT remained elevated in groups A and B, suggesting that HIV infection and residual inflammation contribute to cardiovascular risk by increasing the levels of inflammation biomarkers (such as hs-CRP), pointing to a relationship between the proatherogenic lipid pattern, immune activation, and inflammation.
Mosepele, et. AL, 2017 PLoS One, 2017;12(8):e0179294 2020;15(8):e0237729.	Cross-sectional study	Investigation of the relationship between HIV and carotid atherosclerosis/monocyte activation in virally suppressed PLHIV in sub-Saharan Africa	The study included 208 HIV-positive adults and 224 HIV-negative controls, both without a history of CVD. Clinical history, bilateral carotid ultrasounds to measure carotid thickness and plaque presence, lipid profile, glycosylated hemoglobin (HbA1c), and soluble sCD163 testing were collected from the participants. Based on these tests, analyses were performed to determine the association between serological status, traditional CVD risk factors, sCD163 levels, and carotid intima-media thickness (c-IMT). The study showed that HIV-positive participants had significantly higher triglyceride and sCD163 levels than the control group, but HbA1c was significantly lower. Regarding the presence of plaque, this was more recurrent in HIV-positive patients; however, no significant difference in cIMT was observed between the participants.	The study showed that HIV-infected participants aged 30–50 years who achieved viral suppression did not have higher cIMT compared to HIV-uninfected controls in Botswana, although the prevalence of carotid plaques was higher in HIV-infected participants. No relationship was observed between elevated sCD163 levels and cIMT or the presence of plaque; however, this persistent monocyte activation may influence future cardiovascular risk.
Hillel, et. AL 2012 HIV Med. 2012;13(5):564-576. 2020;15(8):e0237729.	Prospective cohort study	Assessment of the risk of premature cardiovascular disease in HIV-infected children by biomarkers of vascular dysfunction and determination of factors associated with biomarkers.	Two groups of participants were analyzed: one group of 226 HIV-infected children (28.4% met the definition of hyperlipidemia) and another group of 140 children (28.6% met the definition of hyperlipidemia) exposed to HIV but not infected (HEU). Biomarkers of inflammation (C-reactive protein, IL-6, and MCP-1), endothelial dysfunction (sVCAM-1, sVCAM-1, and E-selectin), and metabolic dysfunction (adiponectin) were measured, in addition to anthropometric measurements, body composition, lipids, glucose, insulin, HIV disease severity, and antiretroviral therapy use. The main results show that biomarkers of endothelial dysfunction, sVCAM-1 and sVCAM-1, and biomarkers of inflammation, CRP and MCP-1, are higher in HIV-infected children and were associated with higher HIV viral loads.	It was observed that the HIV-positive group of children had higher levels of biomarkers associated with inflammation, coagulation, and endothelial dysfunction compared to HEU children, mostly independent of metabolic factors such as hyperlipidemia or insulin resistance. These findings suggest that HIV itself can cause immune activation and resulting endothelial injury, and that ART could directly or indirectly (through changes in metabolic profile) increase biomarker levels.

FIGURE 1-2: Review of the Selected Articles.

Publication Data	Type of Study	Aims of the Study	Methods and Results	Conclusions
Lo, et. AL 2014 Open Forum Infectious Diseases, Volume 1, Issue 3 2020;19(3):e227720.	Prospective randomized study	Investigation of the effects of HIV infection and ART on cholesterol efflux in PLWH with acute infection.	The study was conducted in two groups of patients: one group of 9 individuals with acute HIV infection not receiving ART, and another group of 8 individuals with the same condition but receiving ART. Serum samples from the participants were used to measure the cholesterol efflux capacity of genetically modified marine macrophages and markers of inflammation and immune activation. Assess the impact of ART on the immune response. After 12 weeks of the study, a decrease in the logarithm of HIV RNA was observed in both groups, but the decrease was more pronounced in the group receiving ART, and the increase in CD4 count was greater in this group. This change in log-HIV RNA was negatively related to the change in cholesterol efflux in both groups. There was an increase in HDL cholesterol in both groups, with a more significant increase in the group receiving ART. Markers of immune activation and inflammation were positively related to the logarithm of HIV RNA. In vitro tests were also performed to evaluate the effect of ART on cholesterol efflux; however, no improvement in efflux capacity was observed.	It has been shown that HIV likely negatively impacts reverse cholesterol transport in people living with HIV, directly impairing cholesterol efflux from macrophages, predisposing patients to the development of CVD (mainly atherosclerosis). After initiating ART for 12 weeks, a significant increase in HDL cholesterol, cholesterol efflux capacity, and CD4 count was observed, along with a decrease in viroemia and markers of immune activation. Concluding that ART, by suppressing viroemia, helps restore HDL-mediated cholesterol efflux capacity when administered in the acute phase of infection. Virolysis due to increased serum acceptance capacity via HDL cholesterol.
Otero, et. AL 2012 HIV Medicine, Volume 13, Issue 8	Observational study	Investigation on the effect of interruption of ART (activity of CD4 count on plasma biomarkers of inflammation and CVD in PLWH.	The study was conducted in two groups of PLWH: one group directed to treatment continuation (TC) and the other to treatment interruption (TI). One hundred and six patients were enrolled in the STORIS study and 54 were included in this substudy (34 in the TC arm and 20 in the TI arm). Blood samples were collected at 12, 24, and 36 months, and levels of IL-6, MCP-1, sICAM-1, sVCAM-1, sP-selectin, and t-PA were measured in cell supernatants using multiplexed bead-based assays. Total cholesterol, HDL, and triglycerides were measured using standard methods, and LDL was calculated using the Friedewald equation. CD4 T cell counts were performed using flow cytometry, and viral load was determined using real-time PCR. Increases in MCP-1 and sVCAM-1 levels were observed over months 12, 24, and 36 in the TI arm. There was an increase in t-PA in both arms over the months 12, 24, and 36, but it remained below the limit of detection in both arms throughout the study. sP-selectin increased significantly at month 36 in both arms, with a significant increase in the TI arm. No differences were observed in sICAM-1 and triglyceride levels between the arms. CD4 T cell counts decreased in the TI arm throughout the study with no changes in the TC arm, and consequently there was an increase in viral load. Regarding total cholesterol, LDL-C, and HDL-C levels, there were decreases in the TI arm over the months.	Some correlations were observed during the study such as viral load and MCP-1 levels, MCP-1 and baseline HDL-C, sVCAM-1 also showed a negative correlation with HDL-C at baseline and at the three study time points. Viral load correlated negatively with total cholesterol, HDL-C, and LDL-C. Thus, it was observed that ART interruption was associated with endothelial dysfunction (MCP-1 and sVCAM-1), platelet activation (sP-selectin and sICAM-1), and coagulation (t-PA), increased inflammatory biomarkers such as sIC-selectin protein (CRP), and monocyte activation reflecting greater systemic inflammation during treatment interruption and increased triglyceride levels and a reduction in HDL levels, which may increase cardiovascular risk. However, it was observed that resuming ART could mitigate these effects, restoring biomarkers to more favorable levels.
Pereira, et. AL 2012 HIV in Health and Disease 9, 32	Observational study	To explore the relationship between plasminogen-1 (POM) enzyme activity and inflammation and oxidation in PLWH.	A total of 227 HIV-infected participants and 409 HIV-infected controls were selected for the study, where POM enzyme and lactonase activities were measured using two different substrates. Additionally, oxidized LDL and MCP-1 levels were measured by enzymatic assay, HDL, and apolipoprotein A-I concentrations by standard methods, and C-reactive protein by a high-sensitivity immunoturbidimetric method (Biodiagnostic). There was a reduction in POM activity and in HDL, and apolipoprotein A-I levels compared to controls. MCP-1 and C-reactive protein (CRP) levels were significantly elevated in HIV-infected patients, indicating increased inflammation. A significant correlation relationship was observed between POM enzyme activity and MCP-1, and between serum POM lactonase activity and oxidized LDL in HIV-infected patients.	The study suggests that POM activity may be influenced by inflammation and lipid dysfunction in HIV-infected patients. However, it was observed that the relationships between POM activity and oxidized LDL and inflammation are influenced by the substrate used to measure POM, in addition to HIV infection, highlighting the need for more accurate methods to assess a POM in the context of inflammatory diseases. The observed differences may be linked to changes in HDL caused by chronic inflammation or the effects of ART. These changes impact POM activity influenced by the type of substrate used, and indicate a possible fundamental relationship between POM and MCP-1 in the regulation of oxidation and inflammation.

FIGURE 1-3: Review of the Selected Articles.

Discussion and Conclusion

An analysis of the articles selected for this review reveals a considerable correlation between HIV infection and chronic systemic inflammation, leading to an increase in biomarkers associated with inflammation, coagulation, and endothelial dysfunction such as sCD163, MCP-1, CRP, sICAM, sVCAM, sP-selectin, and t-PA [12-15]. MCP-1 (Monocyte Chemoattractant Protein-1) plays an essential role in the inflammatory process, where it functions to activate or increase the expression of other inflammatory factors or cells [16]. In the case of PLWH (People Living With HIV), an effect of HIV on the activation of this biomarker was observed in direct correlation with viral load [12], leading to increased recruitment of non-classical monocytes (CD14–CD16+) on the vascular endothelium surface, differentiating into macrophages that, in the arterial wall, ingest oxidized LDL, promoting the formation of lipid-laden foam cells and secretion of inflammatory cytokines and proteases, favoring the progression of atherosclerosis [17, 18]. The deregulation of inflammatory cytokines resulting from infection provides a pro-atherogenic lipid pattern in PLWH [15], promoting changes in function and decreased HDL levels [19], directly impacting the reverse cholesterol transport process—a mechanism by which cholesterol is removed from peripheral tissues, including vascular walls, through aqueous diffusion, passive diffusion, or active transport mediated by transmembrane proteins, and then transferred to HDL particles that transport cholesterol to the liver, where it is metabolized or excreted. Cholesterol efflux capacity (HCEC) is the ability of HDL to remove cholesterol from the cell, and this

mechanism can be affected by impairment of HDL’s anti-atherogenic properties, contributing to the development of cardiovascular disease (CVD), mainly atherosclerosis [20]. According to Di Yacovo et al., [15], an increase in carotid intima-media thickness (c-IMT) was recorded in PLWH, with or without ART, indicating that HIV infection, mediated by CRP, possibly interferes with this marker, which is considered a predictor of future CVD in the general population. However, this same result was not observed by Mosepele, et al., [14], as the study conducted in Botswana did not identify higher c-IMT values in virally suppressed PLWH compared to the control group, but found that HIV infection may be associated with increased prevalence of carotid plaque. Therefore, other studies should be considered to establish c-IMT as a reliable marker. Viral suppression due to ART reduces immune activation and inflammation and improves lipid phenotypes and markers [15], reaching levels similar to the HIV-uninfected population. However, persistent inflammation was still observed through elevated CRP levels, with other factors such as intestinal microbial translocation, ongoing viral replication, and coinfections possibly contributing to this condition [15]. An increase in cholesterol efflux capacity (HCEC) was observed independently of HDL changes, CD4+ T cells, and monocyte activation markers, indicating that HIV itself and its related proteins may be linked to HCEC alterations and that viral suppression is an important factor for improvement of this parameter [12, 19], observed that interruption of ART up to 36 months can lead to a rapid increase in viral load and consequent increase in biomarkers of immune activation, inflammation, lipid markers, endothelial dysfunction, platelet

activation, and coagulation, as well as a decrease in HDL levels, resulting in systemic inflammation and increased risk of CVD, demonstrating the importance of ART in infection control and consequent reduction in risk of developing other diseases such as CVD. The HDL/Monocyte ratio emerges as a new biomarker studied to indicate prognosis of cardiovascular disease (CVD), such as coronary heart disease (CHD), in the general population, due to its relation to atherosclerosis pathogenesis [18]. Monocytes have a pro-inflammatory effect when circulating, while HDL has an anti-inflammatory effect, exerting a protective role in the atherosclerosis process [21]. However, no articles were found directly relating the ratio between HDL cholesterol levels and absolute monocyte count as a predictor of cardiovascular disease in PLWH. Nevertheless, a negative correlation between MCP-1 levels and HDL concentration was observed according to Olmo et al. [12], as low HDL levels worsen the pro-inflammatory state, contributing to CVD development in PLWH, reinforcing that the HDL/Monocyte marker is a potential biomarker to be considered in future studies to predict CVD development in PLWH, expanding prognostic possibilities especially because it is a cheap and convenient method [18]. Furthermore, from article evaluation, it was possible to infer that ART is essential to mitigate HIV's pro-inflammatory and dyslipidemic effects, and adjuvant treatments to ART should be studied to address chronic inflammation in this population[20].

Final Considerations

HIV infection remains a major global public health issue for which a cure is still unknown. Despite the existence of treatment for

the condition, chronic inflammation and other dysfunctions caused by the virus increase the likelihood of developing other diseases, such as cardiovascular diseases (CVD). The present work achieved its main objective by investigating the HDL/Monocyte ratio as a potential marker to be used as a predictor of CVD in people living with HIV (PLWH). However, gaps in the literature and a scarcity of studies validating the use of this marker in PLWH were identified, possibly because it is a specific population and because research involving this marker in the general population is recent.

A correlation was found between low HDL levels and high levels of inflammatory markers, reinforcing the promising potential of this marker for future investigations, supported by its potential in clinical management as a simple and cost-effective method. Finally, we conclude that it is suggested this marker be considered in future studies that investigate its applicability and sensitivity, in order to facilitate the early diagnosis of cardiovascular diseases in PLWH. Furthermore, this work aims to propose investigations related to complementary strategies to antiretroviral therapy (ART) for controlling chronic inflammation caused by HIV infection, thereby preventing other diseases resulting from this condition in PLWHIV.

Conflicts of Interest

In accordance with Taylor & Francis policy and my ethical obligation as a researcher, I am reporting that I have no financial and/or business interests in a company that may be affected by the research reported in the enclosed paper. I have disclosed those interests fully to Taylor & Francis, and I have in place an approved plan for managing any potential conflicts arising from that involvement.

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