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Review Article

Evaluating the use of antiviral drugs in HIV patients with cardiovascular diseases and how to reduce the incidence of cardiac events in these patients

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Abstract: Globally, the incidence of newly diagnosed human immunodeficiency virus (HIV) infections is concerning. Despite enhancing the quality of life for this patient population, antiretroviral therapy (ART) is linked to an increased risk of cardiovascular disease (CVD). In people living with HIV (PLWH) undergoing ART, recent research has demonstrated that the use of statins and aspirin (ASA) can reduce the incidence or progression of CVD. However, research has demonstrated that interactions may occur when these medications are used concurrently in the treatment regimen of PLWH. Therefore, we conclude this systematic review to evaluate the use of ART in HIV individuals with CVD and also the effect of adding ASA and statins to ART for reducing the cardiac adverse events.

Keywords: Human immunodeficiency virus, antiretroviral therapy, cardiovascular diseases

Introduction

Human immunodeficiency virus (HIV) affects an estimated 37.7 million people worldwide, with sub-Saharan Africa bearing the greatest load of the disease [1]. HIV infection is known to raise the risk of atherosclerotic cardiovascular disease (ASCVD), perhaps due to prolonged immunological activation and inflammation. Pericarditis and myocarditis resulting from pulmonary hypertension, opportunistic infections, cardiac tumours, and pericardial effusion were the most prevalent cardiovascular complications among HIV-positive individuals in developed nations during the 1980s [2].

The life expectancy disparity between individuals living with and without HIV has decreased globally since the introduction of combination antiretroviral therapy (ART), which has resulted in a transformation of the population of people living with HIV (PLWH) [3]. While early epidemics had high mortality rates, PLWH can now anticipate living a lifespan that is close to normal. Increasing efficacy and decreased toxicity of ART were factors in the worldwide decline in opportunistic infections and, consequently, in the reduction of morbidity and mortality associated with AIDS [4]. As a result, the spectrum of HIV-related diseases has shifted significantly from opportunistic instances to those associated with ageing, such as cardiovascular disease (CVD), renal dysfunction, and cognitive deterioration. Also, conventional risk factors such as diabetes, dyslipidemia, and hypertension are more common in PLWH. Furthermore, chronic inflammation and dyslipidemia brought on by HIV infection contribute to the development and progression of atherosclerosis [5]. The ongoing buildup of lipids and inflammation within the arterial wall is what distinguishes atherosclerosis. Reactive oxygen species and oxidative stress are molecular factors that exert a substantial influence on the development of atherosclerosis. Research has demonstrated that both HIV infection and ART contribute to the formation of oxidative stress, a mechanism through which endothelial dysfunction occurs [6].

Moreover, HIV infection induces oxidative stress, which facilitates apoptosis and contributes to the instability of plaques. Atherosclerosis is correlated with hypercholesterolemia and alterations in lipid metabolism. ART has demonstrated substantial effectiveness in viral load

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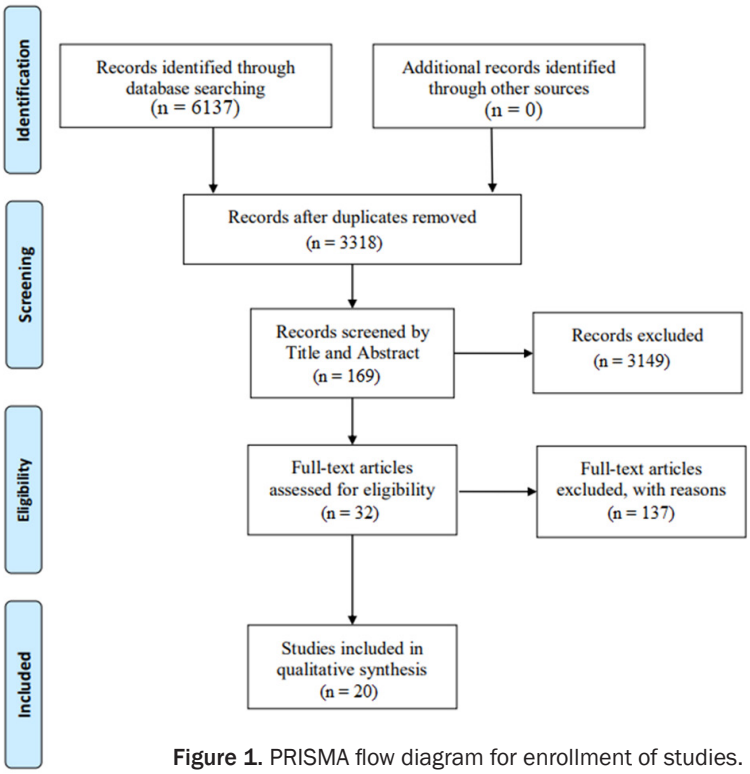

Figure 1. PRISMA flow diagram for enrollment of studies.

The research was performed in compliance with the PRISMA criteria, Preferred Reporting Items for Systematic Reviews and Meta-Analyses, and the Flow Diagram is shown in **Figure 1**. The research was conducted in the PubMed, MEDLINE, Scopus, Web of Science, DOAJ, Science Direct, and Google Scholar databases between January 2019 and October 2023. It used the Advanced Search Builder, and the keywords were searched in [Title OR Abstract]. We have filtered only research articles published in English language and using the terms '(Human Immunodeficiency Virus [Mesh] OR Acquired Immunodeficiency Syndrome Virus [Mesh]) AND (Cardiovascular Disease [Mesh] OR Cardiac Event [Mesh]) AND (Antiretroviral Therapy [Mesh])'.

suppression; however, it is correlated with metabolic disorders such as insulin resistance, diabetes mellitus, and lipodystrophy syndrome. These complications contribute to an elevated risk of CVD among individuals infected with HIV [7]. Furthermore, specific medication combinations utilized in highly active antiretroviral therapy (HAART) may potentially heighten the susceptibility of individuals living with HIV to CVD [8]. Combining lopinavir with ritonavir, which is known to induce dyslipidemia, increases the risk of CVD, thereby demonstrating the adverse effects of the ART regimen in PLWH [9]. On the other hand, recent research has demonstrated that the use of statins and aspirin (ASA) can reduce the incidence or progression of CVD.

Therefore, we conclude this systematic review to evaluate the use of ART in HIV individuals with CVD and also the effect of adding ASA and statins to ART on reducing cardiac adverse events.

Material and methods

Search strategy

We have conducted a literature review of the new update of ART in HIV patients with CVD.

Inclusion and exclusion criteria

Original articles that evaluated the new update of ART on HIV patients with CVD and studies that investigated the reduction of cardiovascular complications in HIV-infected patients undergoing ART were eligible for inclusion in the systematic review. References in selected research were reviewed for other relevant literature. There were both retrospective and prospective investigations, as well as blinded and non-blinded research. Case reports and case series involving a limited number of patients, review articles lacking original data, editorials, letters, and conference papers were all excluded.

Data extraction and quality evaluation

Titles and abstracts were reviewed by Azad Mojahedi. After implementing inclusion and exclusion criteria, data from studies were extracted based on the requirements of the survey.

After scanning the references in previously published review articles, any relevant studies were included. We obtained 17 eligible published research articles in their final version. For some

of them, we chose to include only the main findings that fit the purpose of this review. Data extraction tables based on the final articles' data are shown in **Tables 1** and **2**.

Discussion

Infection with HIV correlates with an increased incidence of CVD. There is a 2.2-fold greater incidence of CVD, such as myocardial infarction (MI) and stroke, among PLWH compared to those without HIV infection [10]. A possible cause for the increased risk of MI following cessation of ART was rebound viremia and subsequent inflammation [11]. It has been discovered that a low CD4 count and uncontrolled viremia duration are associated with worse outcomes and an increased risk of CVD. Furthermore, commencing ART at a CD4 count greater than 500 cells/ul led to a greater increase in a healthy lifespan in comparison to initiating ART at lower CD4 counts [12, 13].

Multiple factors contribute to the pathogenesis of CVD in individuals with HIV, including direct HIV effects, adverse effects of ART, and the gradual accumulation of conventional CVD risk factors that occur with aging. All of these things work by triggering inflammation and throwing off the immune system's balance. Despite the fact that ART initiation restores immunity, immune marker levels do not revert to those observed in healthy individuals without HIV. Immune balance restoration appears to be more effectively achieved with early initiation of ART during HIV infection as opposed to later initiation of ART [14, 15]. The prevalence of conventional CVD risk factors, including smoking, is higher in PLWH compared to non-HIV-infected populations in Western nations [16]. There is a lack of clarity regarding the situation in Sub-Saharan Africa, as reports suggest that the prevalence of CVD risk factors is higher among PLWH compared to the general population, while studies suggest that PLHW have a more favourable CVD risk profile [17].

The mechanisms of HIV in ASCVD

Despite the paucity of evidence regarding ASCVD in PLWH prior to the advent of ART, the few investigations that have documented it are noteworthy [7]. Joshi et al. identified lymphocyte and mononuclear cell infiltration in the vessel walls of three out of six children who perished from acquired immune deficiency syndrome (AIDS); this infiltration is considered a precursor to atherosclerosis [18]. Furthermore, additional post-mortem examinations of young patients aged 23 to 32 who had been infected with HIV unveiled significant atherosclerotic plaques [19]. These initial reports of premature atherosclerosis in the context of HIV/AIDS sparked numerous inquiries to look into the pathogenesis of HIV-mediated ASCVD.

Strong evidence currently exists to support the underlying causes of untreated HIV infection, which results in pro-inflammatory consequences such as intestinal permeability, microbial translocation, and a loss of CD4 T-cells [20]. Acute MI and other ASCVD events are more likely to occur in patients with CD4 T-cell depletion. Moreover, HIV has the ability to impart direct stimulation to the endothelium, leading to an elevation in endothelial permeability and subsequent leukocyte ingress into vessel walls; this ultimately culminates in endothelial dysfunction and vascular inflammation [21].

Extensive evidence suggests that systemic inflammation significantly contributes to the onset and advancement of ASCVD in the general population. C-reactive protein (CRP), a pro-inflammatory biomarker, concentrations in PLWH increase with time, with the biomarker increasing more dramatically in those who progress to AIDS. Interleukin (IL)-6, a cytokine that causes hepatocytes to release CRP, is also higher in PLWH and can be used as another sign of poor health related to CVD and death from any cause [22, 23]. PLWH have been found to have elevated serum concentrations of proprotein convertase/kexin type 9 (PCSK9), a protease implicated in cholesterol trafficking and a contributor to systemic inflammation, in comparison to HIV-negative controls, according to a number of investigations [24].

Despite the fact that ART reduces certain inflammatory markers, numerous markers remain elevated despite the absence of detectable HIV RNA levels. Despite the fact that ART promotes CD4 T-cell recovery and reduces inflammation, there is evidence to suggest that low-level ongoing viral replication continues to occur within lymphoid organs [25]. In an investigation that compared short-term ART use with long-term ART based on CD4 T-cell counts, it was found that groups with higher levels of

Table 1. Characteristics of the included articles evaluating the effect of ART in PLWH on the risk of CVD

Study	Year	Study type	Study population	Study groups	Mean of age, year ± SD (IQR)	Gender, male (%)	Duration of HIV (Years/Months)	Duration of ART (Years/Months)	Initial CD4 cell count (cells/mm^3)	Mean follow-up (Years/Months)	Conclusion
Surial et al.	2023	Prospective cohort study	5,362	1,837 (INSTI-based ART) and 3,525 (other ART).	38.0	4217 (79)	-	-	304	4.9 years	In this simulated target trial, we found no difference between treatment-naïve individuals with human immunodeficiency virus who initiated INSTI-based ART and those on other ART in terms of short-term or long-term risk for CVD events.
Huck et al.	2023	Cross-sectional study	112	37 (HIV cases) and 75 (non-HIV cases).	56.0	76 (68)	17.8 ± 7.0 years	-	682	-	HIV-negative controls demonstrated better coronary microvascular function than PLWH. Changing from dolutegravir/lamivudine/abacavir to bictegravir/emtricitabine/tenofovir alafenamide did not result in an improvement in coronary microvascular function.
Woldeyes et al.	2022	Cross-sectional study	333	-	45 ± 10.4	103 (30.9)	-	10.07 ± 3.9 years	579	10.58 ± 3.9 years	According to the findings of this study, male gender, rising age, a high BMI, and a prior ART regimen of tenofovir disoproxil fumarate, lamivudine, and nevirapine were all associated with an increase in CVD risk factors.
Elvstam et al.	2022	Prospective cohort study	6,562	Suppression (< 50 copies/ml), low-level viremia (50-999 copies/ml), and high-level viremia (1,000 copies/ml).	37 (31-45)	4,150 (63)	-	12 months	240	5.5 years	This study discovered that increasing exposure to HIV viremia was connected to CVD in ART recipients, although persons with low-level viremia had no increased risk when compared to viral suppression.
Majonga et al.	2022	Cross-sectional study	406	195 (PHIV) and 211 (non-HIV cases).	10.75 ± 2.7	203 (50)	-	4.8 years	710	18 months	In comparison to HIV-negative children, children with PHIV had elevated levels of proinflammatory and cardiovascular biomarkers, according to this study. Increased CRP and GDF-15 levels were linked to CVD in PHIV children.
Tiarukkitsagul et al.	2021	Cross-sectional study	460	345 were receiving first-line ART and 115 were receiving second-line ART.	51.2	262 (57.0)	14.7 years	-	509	10 years	First-line and second-line ART groups had a median 10-year CVD risk of 3.0% and 5.1%, respectively. The overall risk of CVD in PLWH, especially for those receiving second-line ART, should be evaluated.
Ounjaijean et al.	2021	Cross-sectional study	60	30 (boosted-PI users) and 30 (non-PI users).	43.7 ± 7.1	34 (56.7)	-	45.8 ± 27.8 months	578	-	The only independent parameter related to variations in CRP, LOX-1, VCAM-1, and OPG is PI treatment. An examination of subgroups revealed that the effects of ART varied among participants who had dyslipidemia.

Njoku et al.	2021	Cross-sectional study	300	100 (HIV cases on HAART) and 100 (HIV cases HAART-naïve) and 100 (controls).	18-59	151 (50.3)	-	4.0 ± 2.4 years	408.43 (HIV cases on HAART) and 250.06 (HIV cases HAART-naïve)	-	According to this study, clinical signs of HIV and the CD4 nadir were more common among HIV-positive and HAART-naive participants. The aortic root, left atrium, and left ventricle dimensions were greater in HAART-exposed individuals, although wall thickness and ejection percentage were higher in HAART-naive individuals.
Temu et al.	2020	Cross-sectional study	541	275 PLWH on ART and 266 non-HIV cases.	43.0 [31-58]	270 (49.9)	-	8.5 years	516		The findings of this investigation suggest that, in addition to established risk factors, monocyte activation may account for the elevated risk of endothelial dysfunction and CVD.
Akkoyunlu et al.	2020	Prospective cohort study	30	-	38.7 ± 10.3	26 (86.7)	-	6 months	476	6 months	Integrase inhibitor-based antiretroviral treatments decrease the oxidative stress caused by HIV infection and may be a good therapeutic option in people living with HIV.
Mogadam et al.	2020	Retrospective cohort study	19	-	48.0 ± 10.0	16 (85)			593		It was found that in HIV-positive people who did not have high blood pressure, diabetes, or any other signs of cardiovascular disease, a lower nadir cluster of differentiation CD4 T-cell count was linked to worse endothelial function.
Muller et al.	2019	Retrospective cohort study	538	-	36.52 ± 10.88	302 (56.1)	-	-	-	5.13 years	The findings of this research indicate that early intervention and preventative measures can help reduce the likelihood of developing cardiovascular diseases.
Pyarali et al.	2021	Retrospective chart review	985	102 (with the history of CVD) and 883 (without CVD).	52.2 ± 11.7	538 (55)	-	-	531	10 years	The conclusion of this study was that CVD risk and prevalence are high among PLWH and that ART treatment could provide protection against CVD. However, primary and secondary preventive medicine utilisation is low.
Yen et al.	2019	Prospective cohort study	121,530	24,306 (PLWH) and 97,224 (matched controls).	32.7 ± 10.0	11,4010 (93.8)	-	-	-	5.86 years	According to the findings of this study, HIV infection is a distinct risk factor for sudden cardiac death, and the incidence of sudden cardiac death is low among PLWH receiving ART.
Yen et al.	2019	Retrospective cohort stud	120,765	24,153 (PLWH) and 96.612 (matched controls).	32.6 ± 9.87	11,3355 (93.8)	-	Within 1 year, 1-2 years, more than 2 years	-	5.83 years	This study found that HIV infection independently predicted incident HF. Furthermore, the risk of HF decreased as the duration of HAART increased.

IQR: Interquartile range, HIV: Human Immunodeficiency Virus, ART: Antiretroviral therapy, PLWH: People live with HIV, BMI: Body mass index, PHIV: Perinatally-acquired HIV, CVD: Cardiovascular disease, PI: Protease inhibitors, HF: Heart failure, HAART: Highly active antiretroviral therapy.

Table 2. Characteristics of the included articles evaluating the effect of using aspirin and statins in PLWH who are receiving ART on the risk of CVD

Study	Year	Study type	Study population	Study groups	Mean of age, year ± SD (IQR)	Gender, male (%)	Duration of HIV (Years/ Months)	Duration of ART (Years/ Months)	Form and dosage of statin	Mean follow-up (Years/ Months)	Conclusion
Grinspoon et al.	2023	Randomized clinical trial	7,769	3,888 (the pitavastatin group) and 3,881 (the placebo group).	50 (45-55)	5,350 (68.9)	-	< 5 years, 5-10 years, and > 10 years	4 mg of pitavastatin	5.1 years	This study discovered that HIV patients who got pitavastatin had a decreased risk of a significant adverse CVD than those who received placebo.
Al-Sayed et al.	2022	Prospective cohort study	181	86 (CSDIs) and 95 (no CSDI).	41 ± 12	132 (73%)	8 years	-	-	3 months	The study revealed that antiretroviral HIV treatments accounted for the highest number of pharmaceuticals implicated in potentially important clinical drug interactions (37%). These were followed by statins (19%), analgesics (11%), cardiovascular drugs (10%), calcium supplementation (5%), and antidepressants/antipsychotics (3%).
Pyarali	2021	Retrospective Cohort study	985	102 (with a history of CVD) and 883 (without CVD).	52.2 ± 11.7	538 (55)	-	-	-	10 years	The utilization of pharmaceuticals for the primary and secondary prevention of CVD was 25% and 44% for statins and 15% and 37% for ASA, respectively.
Trevillyan et al.	2021	Randomized clinical trial	84	44 (rosuvastatin group) and 40 (placebo group).	54.0 ± 6.0	82 (97.6)	17.2 ± 8.5	-	20 mg rosuvastatin or 10 mg on antiretroviral therapy for 96 weeks		This study found that statins given recommendations did not enhance carotid intima media thickness in PLWH but caused serious side effects.
Hearps et al.	2021	Double-blind, placebo-controlled trial	69	33 (Rosuvastatin group) and 36 (placebo group).	54 ± 6.5	68 (98)	19.1 ± 3.65	-	20 mg/day of rosuvastatin for 96 weeks	48 weeks	In terms of HIV virus load, 87% and 92% of statin and placebo patients had viral loads less than 50 copies, respectively.
Negredo et al.	2020	Randomized pilot trial	42	42 PLWH on a PI-based regimen were randomly assigned (1:1) to either transition from PI to Raltegravir (n = 20) or stay on PI (n = 22).	50.6 ± 5.8	34 (80)	-	72 weeks	20 mg/day of atorvastatin for 48 weeks	72 weeks	In this trial, shifting from a PI to Raltegravir and low-dose atorvastatin did not reduce inflammatory or immune activation indicators.

IQR: Interquartile range, HIV: Human Immunodeficiency Virus, ART: Antiretroviral therapy, PLWH: People live with HIV, CVD: Cardiovascular disease, PI: Protease inhibitors.

inflammatory markers were more likely to develop ASCVD in the future [26]. An independent investigation that synthesized data from three global studies involving more than 3,700 PLWH discovered that elevated levels of inflammatory markers at baseline were correlated with an increased risk of developing CVD in the future [27].

The effects of ART on CVD

Although ART has significantly reduced mortality and revolutionized the management of PLWH, it is not without its metabolic adverse effects, which include dyslipidemia, insulin resistance, and overt diabetes mellitus. Currently, scientists are trying to figure out how much the complicated interaction between HIV infection, common heart disease risk factors, and ART makes CVD worse in PLWH [28].

Treatment strategies for HIV have been designed to target distinct phases of the virus's life cycle. In most cases, a first antiretroviral regimen consists of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a third active medication from one of the following classes: protease inhibitor (PI) with a booster (ritonavir or cobicistat), integrase strand transfer inhibitor (INSTI), or non-nucleoside reverse transcriptase inhibitor (NNRTI) [29]. In addition to their substantial benefits, prior research has found that ART has been related to metabolic alterations and an increased risk of CVD, including atherosclerosis. A few antiretroviral medications are known to cause oxidative stress through a variety of metabolic processes. NRTI, for example, causes mitochondrial toxicity, whereas PI stimulates hepatic cytochrome p450. PIs are also linked to dyslipidemia and fibrinogenemia, while NNRTIs elevate total cholesterol and LDL-C [15, 30]. Efavirenz induces hyperlipidemia, which is indicative of the use of HAART and its association with a number of cardiovascular system-damaging effects that result in CVDs [31]. Nevertheless, upon assessing the advantages against the disadvantages, it was demonstrated that ART induces less oxidative stress than HIV infection. As demonstrated by Akkoyunlu et al. [32], PLWH who are on ART have a lower risk profile for CVD than those who are not on ART. This research demonstrated that oxidative stress induced by HIV infection is reduced in integrase inhibitor-based antiretroviral therapy. Given that PLWH require ART for the duration of their lives, an integrase-based regimen may be a more viable alternative. The prevalence of CVD is elevated among PLWH undergoing the HAART regimen, according to the findings of Muller et al. [33], when metabolic alterations are considered in these populations. While the precise origins of these presentations remain unknown, it is hypothesized that they serve to implement individualized treatment and early prevention strategies based on the backgrounds of specific patients [30]. Tiarukkitsagul et al. [34] discovered that among PLWH, the 10-year risk of ASCVD was significantly higher for those on second-line ART (a ritonavir-boosted PI) than for those on first-line ART (an NNRTI-based regimen). It was discovered that second-line ART was an independent risk factor for intermediate to high ASCVD risk at 10 years.

In 2022, Woldeyes et al. [35] conducted a study on 333 HIV-positive individuals who underwent ART. The risk factor that was most frequently identified in 69.4% of cases was dyslipidemia, while in 36.8% of cases, abnormal fasting blood glucose (≥ 100 mg/dL) was detected. Twenty-three percent were diagnosed with hypertension, whereas 11.1% and 22.8% had metabolic syndrome and obesity, respectively. In 95.9% of cases, the Framingham risk score was modest. CVD risk factors were increased with male gender, advancing age, a high body mass index, and a prior ART regimen consisting of tenofovir disoproxil fumarate, lamivudine, and nevirapine. In another study, Delabays et al. [36] discovered that exposure to abacavir and CD4 T cell nadir levels below 200 cells/mm^3 were both HIV-specific factors that were separately related to the development of ASCVD. In 2023, Surial et al. [37] evaluated the effects of INSTI-based ART on CVD in HIV patients. Among 5,362 patients with HIV, 1,837 started INSTI-based ART, and 3,525 started other ART. They found no difference between HIV patients who received INSTI-based ART and those who received other ART in terms of short-term or long-term risk for CVD events. Also, a study conducted by Majonga et al. [38] evaluated the CVD in children with perinatally acquired HIV (PHIV). Among the 406 cases that participated in this study, PHIV- and non-HIV-infected cases were 195 and 211, respectively. According to this study, in comparison to HIV-

negative children, children with PHIV had elevated levels of proinflammatory and cardiovascular biomarkers. Increased CRP and GDF-15 levels were linked to CVD in PHIV children.

The effects of aspirin and statins on HIV patients with CVD

It is the main goal of published ASCVD programmes and national guidelines to help find high-risk PLWH earlier and, if needed, start lipid-lowering therapies along with major lifestyle changes. Acetylsalicylic acid (ASA), often known as aspirin, is a non-steroidal anti-inflammatory drug (NSAID) that has anti-platelet and anti-inflammatory effects [39, 40]. It has been discovered that ASA inhibits the progression of the disease in HAART-naive patients, elevates CD4+ counts, reduces p24 antigen, and improves body weight and hemoglobin levels, among other beneficial effects [41].

Given the considerable advantages associated with aspirin, it is recommended to incorporate this medication into ART. However, the literature indicates that potential concerns may include nonadherence and polypharmacy. When taking aspirin in higher amounts, additional adverse effects such as gastrointestinal (GI) bleeding may occur. This would exacerbate the discomfort experienced by individuals who are pregnant or breastfeeding and require additional precautions [42]. To determine the true advantages of aspirin in PLWH, further research is required to examine the effects of supplementing ART with low-dose aspirin. In the general population, statins are commonly used for primary and secondary prevention of cardiovascular disease. Although they have the potential to prevent CVD in PLWH, clinicians are not prescribing enough of them. The factors contributing to this and their utilization are diverse, spanning from patient-related concerns such as nonadherence and ignorance of the advantages of statins to clinician-level factors such as inadequate understanding of prescribing guidelines [30, 43].

Additionally, interactions between statins and specific ART medications are a critical factor for PLWH to consider. A heightened susceptibility to drug interactions exists among patients who are undergoing treatment with cytochrome P450 inhibitors, including ritonavir and cobicistat. Of all the statins, lovastatin and simvastatin generally have the greatest cytochrome P450 metabolism and should be avoided in PLWH, but pitavastatin and pravastatin are less likely to interact pharmacologically with routinely given drugs [44, 45]. In 2022, Al-Sayed et al. [46] evaluated the potential clinically significant drug interactions in 181 HIV patients who underwent ART. The study revealed that antiretroviral HIV treatments accounted for the highest number of pharmaceuticals implicated in potentially important clinical drug interactions (37%). Following these were statins (19%), analgesics (11%), cardiovascular drugs (10%), calcium supplements (5%), and antidepressants/antipsychotics (3%).

Pyarali et al. [47] conducted a trial in 2021 to evaluate the efficacy of ASA and statins in PLWH receiving ART for the prevention of primary and secondary CVD. Patients receiving ART had a reduced risk of developing CVD. The utilization of pharmaceuticals for the primary and secondary prevention of CVD was 25% and 44% for statins and 15% and 37% for ASA, respectively. In another study, the effect of adding ASA to ART in HIV patients was evaluated. Negredo et al. [48] conducted a randomized pilot trial in PLWH to investigate the benefit of adding atorvastatin to raltegravir. There was not a significant effect on the lipid profile or immunological status as a result of the addition of statins; there was also no reduction in inflammation or immune-related markers. A significant concern regarding the use of statins in PLWH is their potential interaction with ART medications.

In 2019, Grinspoon et al. [49] conducted a study on using pitavastatin to prevent vascular complications in HIV cases, which minimally interacts with ART to prevent CVD. The results of this study indicated that the moderate-intensity pitavastatin (4 mg/day) regimen was more effective than the 40 mg/day pravastatin regimen in reducing low-density lipoprotein C (LDL-C). In 2023, another study was conducted by the same author to evaluate the use of pitavastatin to prevent CVD in HIV cases [50]. Random assignment was performed in this study between a placebo and daily pitavastatin calcium (at a dose of 4 mg) for 7,769 HIV-positive individuals with a low-to-moderate risk of CVD who were undergoing ART. Over a median of 5.1 years of follow-up, they discovered that HIV

patients who received pitavastatin had a lower risk of a significant adverse cardiovascular event than those who received a placebo (P = 0.002). However, in a study conducted by Trevillyan et al. [51], it was found that statins below recommendations did not enhance carotid intima media thickness in PLWH but caused serious side effects.

In 2023, a meta-analysis conducted by Mokgalaboni et al. [52] evaluated whether statin treatment improves or worsens the surrogate markers of HIV infection. No substantial disparities were observed in the CD4 count between the baseline and post-treatment periods, indicating that statins do not have a beneficial impact on these parameters. Furthermore, their research findings indicated that there was no statistically significant correlation between the use of statins and the likelihood of viral rebound (P < 0.00001). Additionally, they discovered a significant correlation between statin use and an elevated indicator of immune activation, which may indicate an increased susceptibility to complications related to HIV (P < 0.00001).

Conclusion

This study summarizes the advantages and disadvantages of ART and highlights the significance of preventing PLWH on ART. We examined HIV patients' CVD manifestations and ART efficacy. According to our findings, ART treatment provides significant advantages for PLWH. Although ART may harm cardiovascular health, it reduces the risk of sudden cardiac deaths as well as heart failure in HIV patients, making it an effective way to reduce morbidity. Also, our findings suggested using ASA and statins along with ART in PLWH to reduce the risk of CVD. However, to demonstrate the efficacy of particular strategies for PLWH on the ART regimen to reduce the risk of CVD, additional research and approaches are required.

Disclosure of conflict of interest

None.

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