

A Review of Arterial Stiffness and HIV Infection in Adult Africans

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Abstract

Aim: To review the impact of the human immunodeficiency virus and antiretroviral therapy on the vasculature.

Objectives: This review seeks to identify the burden which the human immunodeficiency virus and antiretroviral therapy have on the vasculature.

Method: Medline/PubMed and Google scholar were searched. There were over 100 publications reviewed. Some people who worked in similar fields were also contacted. The present review summarized current understanding of Human immunodeficiency virus, antiretroviral therapy and effect on the vasculature such as arterial stiffness. Atherosclerosis, endothelial dysfunction, the strengths and weaknesses of current testing strategies, and their potential applications in clinical research and patient care. The association of inflammatory biomarkers, blood pressure and ageing with arterial stiffness were also reviewed.

Conclusion: Available literature shows that HIV and antiretroviral agents have a great impact on the vasculature and its progression.

Keywords: Human immunodeficiency virus; Antiretroviral therapy; Blood pressure; Aging; Arterial stiffness; Endothelial dysfunction

Introduction

Acquired Immune Deficiency syndrome (AIDS) is a result of the human immunodeficiency virus (HIV) which leads to failure of the immune system [1]. HI virus infects vital cells in the human immune system such as the helper T cells leading to low levels of CD4+ T cells. AIDS related deaths have decreased dramatically for those on antiretroviral therapy (ART) [2]. Before the advent of antiretroviral treatment mortality rate annually in individuals with HIV infection was more than 20 percent but after a decade of treatment, annual mortality globally has been reduced to less than 2 percent [3].

The use of ART, led to new concerns such as that of insulin resistance and increased fat distribution in the body. Insulin resistance resulted in increased incidence of metabolic abnormalities namely dyslipidemia and diabetes mellitus. Cardiovascular disease became an important cause of death in HIV-infected patients [3].

Arterial stiffness describes the reduced capability of an artery to relax and contract in response to pressure changes. Pulse wave velocity (PWV) a measure of arterial stiffness is calculated by measuring time taken for a pulse wave to travel between two set points [4]. Commonly used points are the carotid and femoral arteries because they are superficial and easy to access (Figure 1). Arterial stiffness is said to be associated with atherosclerosis. Arterial stiffness (measured by carotid-femoral-pulse wave velocity) and central augmentation index have been shown to independently predict cardiovascular events, including stroke [5,6].

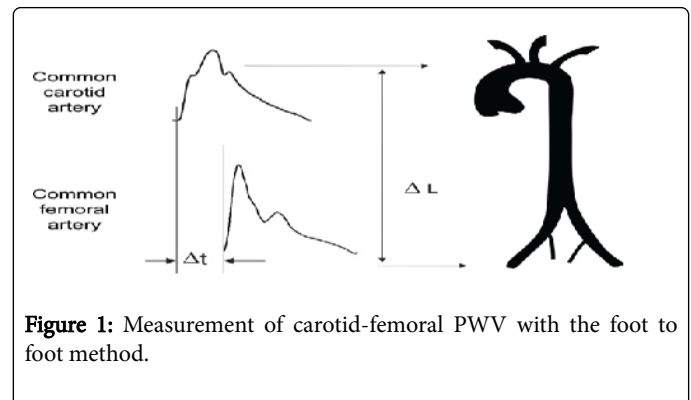


Figure 1: Measurement of carotid-femoral PWV with the foot to foot method.

Some clinical studies have suggested that if HIV is untreated it can contribute to early vascular disease [5-7].

According to the World Health Organization approximately 36.9 million people globally were living with HIV by end of 2014. Two million people became newly infected with HIV by end of 2014 and 1.2 million people died from AIDS-related illnesses. There were 5.8 million people with access to antiretroviral therapy by June 2015. As of June 2015, 15.8 million people living with HIV were accessing antiretroviral therapy, up from 13.6 million in June 2014. Since 2000, around 38.1 million people have become infected with HIV and 25.3 million people have died of AIDS-related illnesses [8].

Despite advances in HIV treatment and prevention many people living with HIV cannot access proper care and treatment. The HIV epidemic affects households, communities, and economic growth of nations. Countries that are hardest hit by HIV also suffer from

infectious diseases, food insecurity, and other problems. Globally efforts have been mounted to address the pandemic. HIV prevalence rates in a number of countries and new infections has declined as a result of prevention [8]. The number of people with HIV receiving treatment in poor countries has increased in the past decade [6,8].

Methods

A literature search of the MEDLINE/PUBMED and Google scholar was viewed from 1996 till date. We included key words such as arterial stiffness and its measurement, HIV, blood pressure, ageing, antiretroviral treatment in the search. In total about 118 studies were extracted and 60 reviewed. Some studies provided data on HIV and the burden of HIV, some provided information such as the impact of HIV and lipids, cytokines, aging, inflammation and the effect of antiretroviral treatment on the vasculature. Studies had data and figures for measurement of arterial stiffness. Two reviewers independently reviewed the abstract and introduction.

Result

From the review most of the studies ascertained that HIV itself causes arterial stiffness and so does the treatment. HIV correlated with age and blood pressure, lipid profile and cytokine levels. Endothelial dysfunction was said to be a prerequisite of arterial stiffness.

The treatment of HIV although has decreased morbidity and mortality but has also increased morbidity in HIV patients. Ischaemic cardiovascular events increasingly occurred in those patients infected for many years with HIV and are attributed either to the infection itself or to the use of HAART.

Discussion

HIV is an important public health problem mostly in the developing world. Our review provides estimates of the burden of HIV in different countries and in different world regions with emphasis on Africa. The review focuses on HIV in relation to arterial stiffness and its complication. The impact of HIV, ART, blood pressure oxidised LDL, cytokines, and aging on arterial stiffness are also discussed. Measurement of arterial stiffness was mentioned.

HIV, arterial stiffness and atherosclerosis

Arterial stiffness is a term for the elasticity of the arteries. The arteries stiffen due to age and atherosclerosis [9,10]. The stiffness, elasticity or compliance of arteries influences the effectiveness of the heart as a pump. Elasticity or compliance of the vasculature is also associated with diabetes mellitus, obesity, pulmonary arterial hypertension, HIV/AIDS and the use of Highly Active Retroviral Treatment (HAART) [11-15] or ART.

Large artery stiffening has been shown to predict future cardiovascular events such as stroke and heart attacks. Arterial stiffness has also been shown to predict parameters such as blood pressure.

Arterial stiffness, measured as pulse wave velocity, is a reliable independent predictor of cardiovascular disease. Arterial stiffness has been shown to be associated with cardiovascular risk factors and atherosclerosis. Meta-analysis reported by some researchers determined that every 1 m/s increase in pulse wave velocity raises the risk of total cardiovascular events by 14% [16,17].

At the 17th Conference on Retroviruses and Opportunistic Infections in February 16-19, 2010 which took place in San Francisco, a presentation by Hsue states that worse levels of inflammation predicted arterial stiffness more than traditional risk factors [18,19]. Hsue again reported that HIV patients with or without viremia have more rapid intima medial thickness (IMT) progression compared to HIV-uninfected controls [19]. Rapid Progression of atherosclerosis which occurred at the carotid bifurcation was linked to inflammation in HIV-infected Patients [20-22]. "These data strongly suggest that inflammation contributes to the higher risk of atherosclerosis noted in HIV-infected persons." In addition it was reported that inflammation was increased in HIV+ individuals, even when viral load was undetectable, and associated with increased CVD risk. Hsue et al. [18] believed their findings "suggest that cardiovascular risk among HIV-infected individuals could be reduced through early initiation of antiretroviral therapy, before CD4 T-cell counts are depressed." They called for prospective studies to test this hypothesis.

Hsue et al. [18,19] also compared people from two cohorts (the SCOPE cohort) in which people in this cohort were started on antiretrovirals whilst they had chronic infections and the other compared study was the OPTIONS study in which treatment was commenced within 6 months of HIV infection. Arterial stiffness was measured as non invasively assessing augmentation index and carotid-femoral pulse wave velocity [19,20,23]. Their data also showed that advanced AIDS with a nadir count of CD4+ T cell count < 350ls ul/ is independently associated with increased arterial stiffnes.

Atherosclerosis (also known as arteriosclerotic vascular disease or ASVD) is a condition in which the arterial wall thickens as a result of accumulation of fatty materials such as cholesterol (Figure 2).

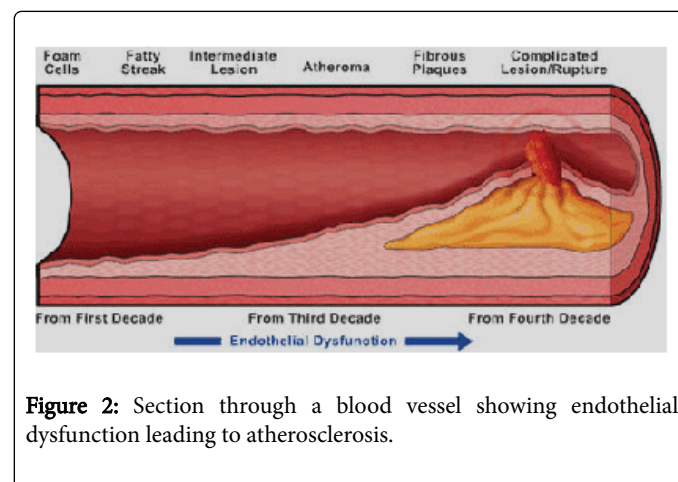


Figure 2: Section through a blood vessel showing endothelial dysfunction leading to atherosclerosis.

Kim et al. [24] in their study found out that the progression of atherosclerosis is due to endothelial dysfunction and starts early in life [25,26]. This might lead to stroke, myocardial infarction and other cardiovascular diseases. Some authors have noted that HIV-infected patients have higher rates of atherosclerosis than HIV negative persons [25,26]. Increased mortality in younger HIV infected patients may be because they develop atherosclerosis earlier, which increases the risk of cardiovascular disease [27,28]. HIV and antiretroviral therapy might induce changes in the lipid profile and insulin resistance leading to the development of atherosclerosis [29-32]. These are recognized risk factors for cardiovascular disease and development of atherosclerosis.

HIV infection may also lead to changes in the endothelium of the blood vessels which leads to depressed immunity, sustained inflammation, and viral replication. These assumptions are supported by recent studies that have shown that interruption of antiretroviral treatment or its intermittent administration increases cardiovascular risk [25,26]. Studies have also shown HIV patients showed higher incidence of insulin resistance and metabolic syndrome [32-34].

Some studies have shown an increased arterial stiffness in HIV infected patients who were not receiving ARV therapy [34].

Cardiovascular disease, arterial stiffness

High blood pressure, high cholesterol, overweight/obesity, tobacco use, lack of physical activity and diabetes are modifiable cardiovascular risk factors that lead to cardiovascular disease. Age gender and family history are non-modifiable risk factors. Thirteen percent of cardiovascular risk factor global deaths are due to hypertension which is followed by tobacco use (9%), hyperglycemia (6%), lack of exercise (6%) and increased body weight and obesity (5%) [35-37].

Currently, the preferred methods for assessing cardiovascular risk are non-invasive. They are easy to apply and allow investigation of a large number of people. The evaluation can be made by ultrasound methods determining intima-media thickness and pulse wave velocity. Such measurements include arterial stiffness measurement using the SphygmoCor, intima media thickening (IMT). The Gold standard for measuring arterial stiffness is the pulse wave velocity using arterial stiffness [38-40].

Ischaemic cardiovascular events increasingly occur in those patients infected for many years with HIV and are attributed either to the infection itself or to the use of HAART. Proportions of HIV infected patients dying of other causes have increased [41,42]. A study of death certificates in New York City showed that the proportion of deaths among HIV-infected patients due to non-HIV-related causes increased from 19.8% to 26.3% between 1999 and 2006. This reflected mortality resulting from cardiovascular disease and non-AIDS-defining cancers. Amongst individuals aged 55 years or above, cardiovascular disease was the leading cause of death. Studies have also shown an increase of myocardial infarction (MI) in HIV populations thus HIV infection being considered as a partial CVD risk factor in these studies [42-44].

Antiretroviral therapy, HIV and cardiovascular disease

In the UNAIDS global report of 2015, 41% of all adults living with HIV accessing treatment in 2014 was up from 23% in 2010 globally. 32% of all children living with HIV accessing treatment in 2014 were up from 14% in 2010. 73% of pregnant women living with HIV had access to antiretroviral medicines to prevent transmission of HIV to their babies in 2014 and new HIV infections among children were reduced by 58% from 2000 to 2014 [8].

Antiretroviral therapy has reduced the risk of early death from opportunistic infections and extended the lifespan of people infected with the HIV. The HIV Outpatient Study (HOPS) reported that there was decrease in HIV-related morbidity and mortality, presumably because of the improved treatment against infections, and the introduction of a combination of antiretroviral therapies (highly active antiretroviral therapy (HAART) [45]. Grunfeld et al. [45] mentioned that in the era before HAART the only metabolic abnormality noted in AIDS was the hypertriglyceridaemia associated with a wasting syndrome [46]. This, he attributed to high levels of cytokines

accompanying chronic infection. Since the advent of effective antiretroviral therapy, infection with the human immunodeficiency virus has been transformed in the western world to a chronic disease associated with a variety of metabolic complications. The lives of individuals infected with HIV who have access to combination antiretroviral therapy (ART) are substantially prolonged, which increases the risk of developing non-AIDS co morbidities, including coronary heart disease (CHD). UNAIDS global report of 2015 states that In Europe and the USA, individuals with HIV infection have a 1.5-fold increased risk of myocardial infarction relative to uninfected individuals. In Europe and the USA, people living with HIV infection have a ~1.5-fold increased risk of myocardial infarction compared to uninfected individuals. In Africa, myocardial infarction risk is unknown, but increased access to ART suggests that rates of CHD will rise in Africa [7,8,46-50]. Grunfeld [42] also stated that atherogenesis in HIV is affected by complex interactions between traditional and immune risk factors. Antiretroviral therapy has varied regimen-specific effects on metabolic risk factors. Overall, ART seems to lessen proatherogenic immune activation, but does not eliminate it even in patients in whom viraemia is suppressed. He suggested that current strategies to decrease the risk of CHD in individuals infected with HIV include early initiation of ART regimens with the fewest metabolic adverse effects, and careful management of traditional CHD risk factors throughout treatment. Future strategies to prevent CHD in patients with HIV infection might involve the use of HIV-tailored CHD risk-prediction paradigms and the administration of therapies alongside ART that will further decrease proatherogenic HIV specific immune activation.

Islam et al. [50] in 2012 conducted a systematic review and meta-analysis of studies comparing the risk of cardiovascular disease between HIV-positive and HIV-negative individuals [51]. They searched the Medline database for relevant journal articles published before August 2010. The studies included comparing the risk between people taking antiretroviral therapy and those who were treatment naive; research comparing the risk between classes of antiretroviral drugs; and studies exploring the association between specific drugs and the risk of cardiovascular disease [51]. A total of 23 studies, including two randomized-controlled trials, met the investigators' inclusion criteria. Three studies looked at the overall cardiovascular risk of HIV-positive people. Their pooled results showed that, compared to HIV-uninfected controls, HIV-positive people had a higher relative risk of cardiovascular disease (RR=1.61; 95% CI, 1.43-1.81; <0.001). Three studies (compared risk between people taking antiretroviral therapy and HIV-negative controls). Their pooled results showed that participants taking HIV treatment had twice the relative risk of cardiovascular disease (RR=2.00; 95% CI, 1.70-2.37; p<0.001). "In summary the risk of CVD is two times higher among ART-treated PLHIV (people living with HIV) than HIV-uninfected people". They concluded that PLHIV are at increased risk of cardiovascular disease. Islam et al. [50] also concluded that although effective in prolonging survival, ART (in particular PI-based regimens) is related to further increased risk of CVD events among people at highest initial absolute risk of cardiovascular disease.

Cerrato et al. [51] stated that HIV patients are exposed to a higher risk of adverse cardiovascular events, due to complex interactions between traditional risk factors and HIV infection itself in terms of ongoing endothelial dysfunctional immune activation/inflammation and increased risk of thrombosis. In his article he critically analysed the current knowledge of pathological and clinical aspects pertaining to the increased risk of cardiovascular events associated with HIV [52].

He also analysed 4159 HIV-positive people who were included in the Keiser permanent database which took place between 1996 and 2001, the hospitalisation rate for coronary artery disease (CAD) as well as the incidence of acute myocardial infarction (AMI) were significantly higher than in HIV-negative participants (6.5% vs. 3.8%, $p=0.003$; 4.3% vs. 2.9%, $p=0.07$ respectively).

Triant et al. [52] had a larger cohort with almost 4000 HIV-infected patients and more than one million controls [53]. They reported acute myocardial infarction (AMI) in 189 HIV and 26 142 non-HIV patients with an increased rate of AMI per 1000 person-years in patients with HIV versus those without HIV (11.13% (95% CI 9.58% to 12.68) vs. 6.98% (95% CI 6.89% to 7.06%). This was after adjusting for age, gender, race, hypertension, diabetes and dyslipidaemia. HIV-associated dyslipidaemia, endothelial dysfunction and inflammation have been proposed as potential risk factors [54,55].

The Joint United Nations Programme on HIV/AIDS, (UNAIDS) global statistics of 2015 states that in 2014, 1.2 million (980,000–1.6 million) people died from AIDS-related causes worldwide compared to 2 million (1.7 million–2.7 million) in 2005 [8].

ART use has increased the quality and length of life of people living with HIV [56-59]. Reasons for the increased risk of CVD among HIV-infected people are not very well known and require considerable attention as CVD is likely to be one of the major conditions to be confronted in the future by populations of people living with HIV.

Before the introduction of HAART the cardiovascular disease manifested are dilated cardiomyopathy, pulmonary hypertension, pericardial effusion, endocarditis, myocarditis and drug-related cardiotoxicity. Some studies by Hsue et al. [18,19] and Barbaro and Klatt [60] suggest that by improving the immunologic state of the patients. There might also be about 30% reduction in the incidence of cardiomyopathy and about 50% in the incidence of cardiac involvement by Kaposi's sarcoma and non-Hodgkin lymphoma with the use of HAART [60,61]. HAART has been shown to cause metabolic syndrome in a high proportion of HIV-infected patients and this may be associated with an increased risk for cardiovascular disease (about 1.4 events per 1000 years of therapy according to the Framingham score) [60,61].

Some international studies including those of Mondy et al. [62] Grundy et al. [63] have implicated the HIV itself and anti-retroviral therapy (ART) as potential mediators of this increased risk of CVD [62-64]. Few studies such as those of Ntsekhe et al. [64] evaluated the prevalence of traditional cardiovascular risk factors among HIV positive patients in sub-Saharan Africa and suggested that rates are significantly lower than in developed countries but some of this difference may be attributed to under diagnosis based on low clinical suspicion and small sample sizes [65].

Cardiovascular risk factors and HIV in Africa

It is estimated that outside Africa the incidence of HIV-associated vasculitis is less than 1% [65]. It was reported by Ntsekhe et al. [64]. That large-vessel vasculopathy involving the aorta or its major branches was increasingly being recognized in young African subjects [65]. These young Africans had no evidence of atherosclerosis, syphilis or other causes of vasculitis. The large vessel vasculopathy was said to occur at a relatively early stage of HIV disease (median CD4 count $370 \times 10^6/L$).

At present older populations in sub-Saharan Africa have increased proportion of CVD being due to chronic and non-communicable diseases. The region is under-represented in studies examining the relationship between HIV and CVD risk factors [65-70]. Mutimura [68] in Kigali, Rwanda suggested an increasing incidence of HIV-associated cardio metabolic syndrome (CMS), in developing countries especially in urban settings [69,70]. The increased access to HAART is expected to result in higher prevalence of cardiometabolic syndrome (CMS) in developing countries where HIV infection is prevalent.

The majority of the articles in Africa examined aspects of pericardial disease in HIV infected African subjects [71].

Appropriate evaluation and intervention programmes need to be implemented in the developing world, especially sub-Saharan Africa, to curtail HIV-related CMS. This intervention should include routine cardiovascular risk assessments, the management of HIV infection with more "metabolically friendly" HAART, and encouragement of lifestyle modifications, particularly smoking cessation, weight management, importance of regular exercise, and a healthy diet.

Arterial stiffness and its measurement

Recently, the role of arterial stiffness has been emphasized in the development of cardiovascular (CV) diseases. Therefore the assessment of arterial stiffness is now increasingly being used in the clinical assessment of patients in some centres [72-74].

Pulse wave velocity is considered a non-invasive diagnostic test for subclinical atherosclerosis (SA) or arterial stiffness, and is a predictor of cardiovascular risk and also a surrogate marker of vascular disease [72-75]. Central pressure, Augmentation index (AIx) and PWV cannot be used interchangeably as indexes of arterial stiffness. PWV is a direct measure of arterial stiffness; central pressure and the AIx are indirect surrogate measures of arterial stiffness [75,76]. They thus provide additional information concerning wave reflections. It will be more reliable if central pulse-wave analysis is coupled with measurement of aortic PWV [70-77].

Until now, there have been very few studies using PWV to evaluate SA or arterial stiffness in HIV patients, and these studies involved very few subjects with conflicting results [77].

HIV, inflammation and endothelial dysfunction

There is considerable data on the role of persistent low grade inflammation in the development of large arteries stiffness [78-80]. Chronic inflammation as a result of HIV infection may explain the association between HIV infection and increased arterial stiffness [81]. Inflammation has also been reported to contribute to the development of cardiovascular disease [81-83]. Endothelial dysfunction is characterized by a reduced ability of vessels to vasodilate. This is accompanied by accumulation of platelets, fibrin and monocytes over an injured endothelium. The injured endothelium will then release substances such as platelet derived growth factor (PDGF), and tissue growth factor B, (TGF-B). These factors will stimulate the proliferation of smooth muscle and the production of connective tissue [84-87].

Activated macrophages associated with HIV may predispose subjects to endothelial dysfunction and may therefore form atheroma.

Both endothelial dysfunction and arterial stiffness are considered risk factors for cardiovascular disease.

Atherosclerosis develops from low-density lipoprotein molecules becoming oxidized (LDL-ox) by free radicals, particularly reactive oxygen species (ROS). LDL is formed in the early stages of atherosclerosis, while ox-LDL is formed in the later stages [87-90]. LDL binds to LDL receptor and ox-LDL binds to scavenger receptor, but the vascular effects of minimally modified LDL and ox-LDL are similar. They both activate endothelial cells, smooth muscle cells and monocytes. Ox-LDL also induces a vasoconstrictor state by reducing the formation of the endothelium-derived vasodilators nitric oxide and prostaglandin while enhancing the production of the vasoconstrictor endothelin-1 (ET-1) [87-90]. The damage caused by the oxidized LDL molecules triggers a cascade of immune responses which with time produces an atheroma.

To clear the lipids, the macrophages attach the lipoproteins to the scavenger receptors which result in the formation of foam cells. The formation of foam cells is the hallmark of atherosclerotic lesions. Ox-LDL is chemotactic for monocytes and T-cells. Lack of the LDL receptors responsible for endocytosis is seen in patients with familial hypercholesterolemia, where they have an abundance of arterial lesions and multiple xanthomata containing foam cell-rich lesions [87-90].

Atherosclerosis affects the entire artery tree, but mostly larger, high-pressure vessels such as the coronary, renal, femoral, cerebral, and carotid arteries. These are termed "clinically silent" because the person having the infarction does not notice the problem and does not seek medical help, or when they do, physicians do not recognize what has happened. The main cause of atherosclerosis is yet unknown, but it is thought to be initiated by inflammatory processes in the vessel wall in response to retained low-density lipoprotein (LDL) molecules.

HIV, blood pressure and arterial stiffness

Some studies have shown an increase in blood pressure associated with the use of antiretrovirals. In a study, increased blood pressure in HIV-infected individuals was associated with established risk factors for hypertension [91-95]. Vessel compliance basically modulates blood pressure to keep it within a relatively narrow range, given that the heart is an intermittent pump. Without compliance, the blood pressure will peak and crash with every beat. Diseased aorta vessels are less elastic/compliant, therefore they cannot modulate blood pressure effectively, hence systolic pressure increases, diastolic pressure decreases and pulse pressure increases [91-95]. This consequently enhanced arterial stiffness.

Arterial stiffness and aging

Age is a significant risk factor for cardiovascular disease [96]. Various strategies, especially controlling hypertension, show benefit in preventing, delaying or attenuating vascular aging. Some other studies have also referred to arterial stiffness as being affected by age [97,98]. Charakida et al. [99] reported that HIV-infected children have been shown to have vascular dysfunction that may be an early step in the development of atherosclerosis. In the study, there was no difference between children receiving antiretroviral therapy and never-treated patients. Vascular aging is accelerated by coexisting cardiovascular risk factors, such as hypertension, metabolic syndrome and diabetes. In a study in which 83 HIV-infected children with a mean age of 10.0 years and 59 controls aged 12.2 years were enrolled. The HIV-infected children had increased arterial stiffness compared with healthy children [99]. These changes were more pronounced with increasing

age in HIV-infected children particularly in those who were receiving HAART.

The Framingham study reported that with advancing age, arterial stiffness and wave reflections increase and elevate systolic and pulse pressures [100].

Long-standing arterial pulsation which might be due to aging in the central artery might cause elastin fiber fatigue and fracture. Increased vascular calcification and endothelial dysfunction are also characteristic of arterial aging. These changes lead to increased pulse wave velocity, especially along central elastic arteries, and increases in systolic blood pressure and pulse pressure [101-104]. Vascular aging is accelerated by co-existing cardiovascular risk factors, such as hypertension, metabolic syndrome and diabetes. The major parameters to be taken into account, when evaluating the degree of arterial stiffness, are; age, blood pressure, and, to a lesser extent, gender and classical cardiovascular risk factors [102-104].

Aging is an important determinant of cardiovascular risk and is associated with a number of changes in the structure and function of the cardiovascular system including the large arteries [101-104]. The aorta plays a vital role in buffering and smoothing the pulsatile nature of blood flow as it travels to the periphery. The aorta stiffens, dilates, and becomes tortuous with increased age. Leading to an increase in pulse pressure, which places additional strain on the aorta and thus limiting its buffering capacity. In addition to vessel wall thickening, aging is associated with a gradual increase in central artery lumen diameter; 9% per decade from 20 to 60 years in the ascending aorta although some recent studies have suggested this does not occur [103,104]. Elderly people are predisposed to lose arterial elastic laminae and increase collagen depot. In a study carried out by Guerin et al. [104] stiffness of the whole aorta was greatest in older subjects, and the impact of age was most marked in those older than 50 years of age [104]. The prevalence of hypertension increases with age, such that greater than 60% of people older than age 65 years are hypertensive with systolic blood pressure >140 mm Hg and/or a diastolic blood pressure >90 mm Hg. Association of aging with arterial stiffness is also evidenced in HIV patients [31,32].

Conclusion

From the reviews there is evidence that arterial stiffness is increased in HIV treatment-naïve patients and those who are on treatment. The HIV increases the chance of having cardiovascular disease and one can describe this as a risk factor although there are some conflicting results. Arterial stiffness therefore provides a conceptual background for increased cardiovascular risk observed among HIV-infected individuals regardless of antiretroviral treatment. Factors such as increased blood pressure, aging, metabolic syndrome were reported to affect arterial stiffness in HIV patients both on treatment and those who are treatment naïve.

Close monitoring by non-invasive evaluation of preclinical atherosclerotic disease should be considered for HIV patients, especially those with additional risk factors for cardiovascular diseases, with the aim of addressing intensive lifestyle and pharmacological interventions aimed at reducing cardiovascular risk. Statins and aspirin should be added to the treatment of those with dyslipidaemia.

The management of cardiovascular risk factors among HIV positive patients needs to be improved. Pulse wave velocity and the augmentation index (AIx75) are two major non-invasive methods of

assessing arterial stiffness. The PWV has been proposed as the gold standard for arterial stiffness measurement. Research efforts need to be directed at lipids and cytokines in case one can find an inhibitor to the cytokines which could help in modelling the endothelium.

There is need for collaborative studies between clinicians and basic science researchers to bridge the gap in respect to paucity of information on HIV and cardiovascular diseases. Results from such studies will prevent and ameliorate the severe cardiovascular consequences in our HIV population.

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