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HIV/AIDS and Coronary Heart Disease on a Collision Course? Review of Zimbabwe

Danai Tavonga Zhou[1,2,*], Olav Oktedalen[3], Tawanda Chisango[4], Babill Stray-Pedersen[1]

[1]Institute of Clinical Medicine, University in Oslo, Oslo University Hospital, P.O. Box 1171, Blindern, 0318 Oslo, Norway
[2]University of Zimbabwe, College of Health Sciences, Department of Medical Laboratory Sciences, P. O. Box AV 178, Avondale, Harare, Zimbabwe
[3]Department of Infectious Diseases, Oslo University Hospital, P.O. Box 4950, Nydalen, 0424, Oslo, Norway
[4]Chinhoyi University of Technology, PO Box 7724, Chinhoyi, Zimbabwe
*Corresponding author: d.t.zhou@medisin.uio.no

Abstract There are very few published manuscripts on coronary heart disease (CHD) from Sub-Saharan Africa (SSA) and Zimbabwe. In fact the few published papers on the subject suggest that CHD is rare in SSA and in Zimbabwean individuals both before HIV and in the era of HIV/AIDS and antiretroviral therapy (ART). However a look at recent literature and data from publications by both the World Health Organization (WHO) and Zimbabwe Ministry of Health and Child Care point towards an epidemiological transition, as CHD is now one of the top causes of death in Zimbabwe. This may be due to the fact that CHD is a complex inflammatory disease involving smoking, obesity, diabetes, atherogenic lipid levels, cytokines and other inflammatory markers such as C reactive protein (CRP) and myeloperoxidase (MPO) and many of these factors have consistently been linked to changing lifestyle as populations move into urban settings. On the other hand, atherogenic lipids and elevated inflammatory markers are more common in HIV infected individuals due to the virus and ART. Hence it is likely that the burden of non-communicable diseases (NCDs) and CHD will increase over time as a result of both urbanization in the general population and a high HIV disease burden in Zimbabwe, pointing towards a collision of HIV and CHD in future.

Keywords: *CHD, epidemiological transition, HIV, NCDs, Zimbabwe*

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1. Introduction

Since 1990, more people have died from coronary heart disease (CHD) than from any other cause globally though death rates are lower in populations with short life expectancies. [1] Death rates differ by region or country because of differences in patterns of smoking, alcohol abuse, physical inactivity, diet, dyslipidemia, hypertension, and genetics. [1] There are reports of decreases in CHD risks in Western countries due to prevention strategies hence most future increase in CHD mortality will occur in developing countries like Zimbabwe, as health and environmental conditions gradually change. [1,2] Exposure to infectious diseases are likely to be superseded by exposure to risk factors for chronic diseases, such as unhealthy diet and lifestyle, accompanied by decline in infant or child mortality and an increase in life expectancy in the general population in our setting. [3] Hence major causes of death and disability will change in a few years while chronic and non-communicable diseases (NCDs) such as cardiovascular disease and cancer will become as important as the infectious diseases causing a major epidemiological transition. [3,4]

The Zimbabwean Ministry of Health and Child Care lists the top causes of death in the country, and there is a clear demonstration that NCDs are becoming as important as communicable diseases in Zimbabwe. [5] Though HIV/AIDS remains number 1, CHD is now number 4 cause of death, ahead of malaria and tuberculosis. [5] A unit to deal with NCDs has been in existence within the Zimbabwean health ministry since 2011 but intervention strategies to reduce CHD have been competing with HIV, TB and malaria. [6] The purpose of this review is to fuel discussion by the public, policy makers, researchers and health practitioners about whether there is need to proactively confront the challenge of increasing CHD in the context of an epidemiological transition, HIV/AIDS and increasing ART exposure in the Zimbabwe setting.

2. CHD Risk Profile for Sub-Saharan Africa

Though CHD remains relatively uncommon in Sub-Saharan Africa (SSA), there is an increasing prevalence of risk factors and CHD incidence. The pace and direction of economic development, rates of urbanization, and changes in life expectancy resulting from the impact of pre-transitional diseases and violence are major determinants of a future CHD epidemic in SSA. [7] A recent change in posture by World Health Organization (WHO) Regional

Office for Africa, with greater focus on NCDs, the United Nations high-level meeting on NCD prevention and control in New York in 2011 and a report from the 30th anniversary of the Pan-African Society of Cardiology conference are good indicators of the recognition of the importance of NCDs and the rapidly unfolding epidemiological landscape. [7]

3. CHD Risk in Zimbabwe

There is a general epidemiological transition in developing countries such as Zimbabwe due to lower death rates, longer life expectancy and urbanization. [7] To compound the problem Zimbabwe has a high HIV/AIDS disease burden with a prevalence of 14.4%, making it fifth in the world in terms of HIV prevalence. [8] As a result there has been rapid scale-up of antiretroviral therapy (ART) with coverage reaching 77% of those requiring ART. [9] Clinical observations have documented increased CHD risk due to dyslipidemia in patients with symptomatic HIV and AIDS. [10] Pathophysiology of dyslipidemia and CHD in HIV positive individuals involves systemic inflammatory processes due to persistent viremia and alteration of enzymes and transport proteins involved in lipid metabolism. [11] No doubt ART has improved the morbidity and mortality of patients. On the other hand, ART has contributed to a multiplicity of adverse reactions in some patients in western countries including dyslipidemia, metabolic syndrome, diabetes and hypertension setting a collision course for HIV/AIDS and CHD in many countries with a double burden of HIV and CHD. [11] Very few studies have been carried out in Zimbabwe on CHD risk and lipid profiles prior to HIV and also in the era of HIV and ART which may lead to the erroneous belief that CHD risk is insignificant in Zimbabwe. [12] The latest study on CHD risk burden from the PURE study reported that people living in high-income countries such as Canada, Sweden and the United Arab Emirates had the highest CHD risk burden while those living in low-income countries such as Bangladesh, Pakistan and Zimbabwe had the lowest risk f burden. [12] Paradoxically, however, fatal and other major CHD events such as myocardial infarction, stroke and heart failure were less common in developed countries than developing countries. [12]

Table 1. Zimbabwe Ministry of Health and Child Care Top 20 Causes of Death, 2016 [5]

Position	Cause of death	Death Rate/100 000
1	HIV/AIDS	1 134.87
2	Stroke	107.75
3	Influenza & Pneumonia	92.45
→4	Coronary Heart Disease	90.05
5	Tuberculosis	81.09
6	Malaria	45.78
7	Diarrhoeal diseases	42.33
8	Diabetes Mellitus	37.33
9	Maternal Conditions	35.39
10	Lung Disease	31.11
11	Low Birth Weight	21.78
12	Cervical Cancer	21.14
13	Road Traffic Accidents	19.27
14	Kidney Disease	17.48
15	Violence	16.88
16	Hypertension	15.87
17	Birth Trauma	15.57
18	Measles	13.83
19	Endocrine Disorders	12.21
20	Prostate Cancer	10.87

According to 2014 WHO data CHD deaths in Zimbabwe reached 2.22% of total deaths, while the age adjusted death rate was 41.17 per 100 000. [13] In 2016 Zimbabwean Ministry reported that the age adjusted CHD death rate was 90.05 per 100 000 or double of the WHO data (Table 1). [5]

4. Zimbabwe Country Profile

Zimbabwe is a landlocked country in the Sub-Sahara African region; bordered by Mozambique South Africa, Botswana, and Zambia (Figure 1). Zimbabwe has a population around 13 million, with 1.56 million people living in the capital Harare. The climate is a blend of cool, dry, sunny winters and warm, wet summers. [14] Zimbabwe has abundant natural resources, including 8.6 million hectares of potentially arable land and more than 5 million hectares of forests, national parks, wildlife estates and natural tourist attractions such as Victoria Falls and Great Zimbabwe (Figure 2 and Figure 3). The economy is diversified but biased toward agriculture and mining, which are by far the country's major foreign-currency earning sectors. In recent years the Zimbabwean agricultural sector and mining industry have faced challenges such as poor irrigation, unaffordable inputs, frequent power outages, inefficient infrastructure, flight of skilled workers, and shortages of funds for working capital and recapitalization. [14] The economy of Zimbabwe shrank significantly after 2000, resulting in a desperate situation for the country with widespread poverty and a high unemployment rate. [16] The government of Zimbabwe continues to face a number of difficult economic problems, including infrastructure and regulatory deficiencies, ongoing indigenization pressure, policy uncertainty and a large external debt burden. [17]

Figure 1. Map of Africa showing the position of Zimbabwe [15]

Figure 2. Victoria Falls

Figure 3. Great Zimbabwe

5. Zimbabwe Unemployment Rates

According to the CIA World factsheet unemployment rate in Zimbabwe has been on an upward trend since the early 2000s using both CIA definition and Zimbabwean definitions (Figure 4). [17,18] The level of unemployment varies markedly by definition because the CIA defines unemployment as the percent of the labor force that is without jobs together with the underemployed while local definitions consider those in self-employment as being employed and define unemployment as number of people actively looking for a job as a percentage of the labor force. [17,18] By whatever definition unemployment rates are above 10% in Zimbabwe and this is worrying in our context because as far back as 1979, a study by Brenner found that for every 10% increase in the number of unemployed there is an increase of 1.2% in total mortality, a 1.7% increase in cardiovascular disease, 1.3% more cirrhosis cases, 1.7% more suicides, 4.0% more arrests, and 0.8% more assaults reported to the police. [19]

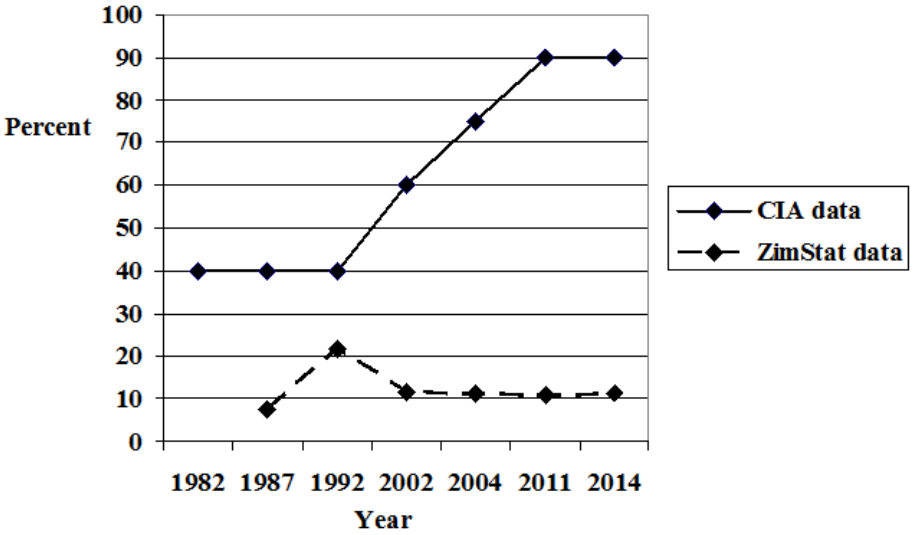

Figure 4. Zimbabwe Unemployment Rates, Adapted from Central Intelligence Agency (CIA) data [17] and Zimbabwe Statistics (ZimStat) Data [18]

6. Zimbabwe Trends in Mortality and Population Growth Rates

According to the 2010-2011 Zimbabwe demographic health survey mortality levels increased slightly in the 1980s and early 1990s, surged in the mid to late 1990s, and then declined in the early 2000s. [6] Due to the HIV epidemic the annual population growth rate dropped from a peak of 4% in 1983 to its lowest (0.65%) in 2003 (Figure 5), [20] while the population was 11.6 million in 2002 and rose gradually to 15.5 million in 2016. [21]

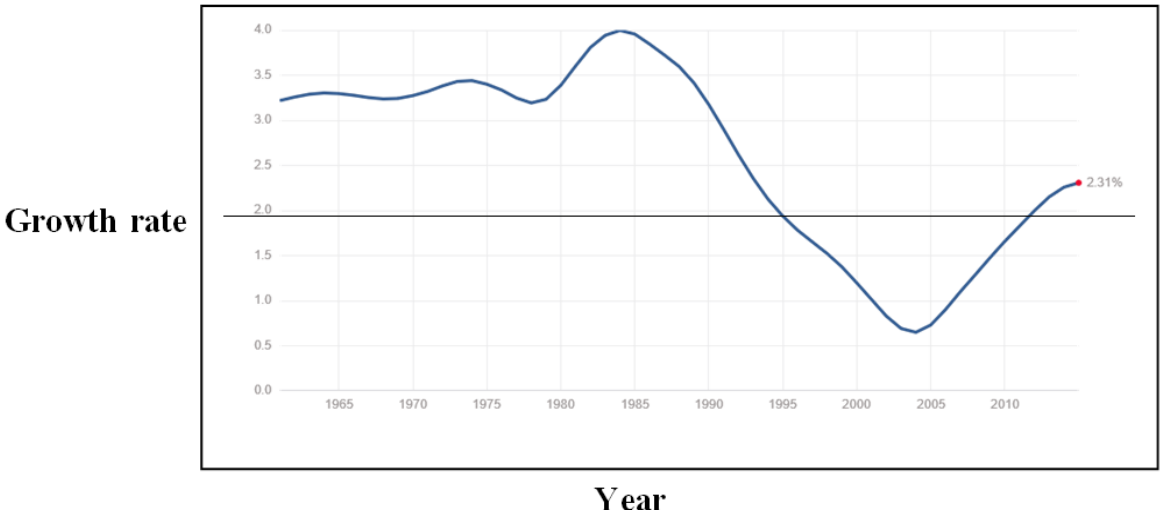

Figure 5. Zimbabwe population growth rates (1965 to date) [20]

7. Urbanization in Zimbabwe

Since 1980 there has been an explosion of an urban population as country laws were changed to recognize the rights of the black majority in Zimbabwe. The transition to majority rule in 1980 saw the lifting of decades of racial restrictions to the "Right to the City" and the urban population of Zimbabwe rose rapidly from 23% in 1982 to almost 40% in 2011. [22] It is estimated that urbanization will continued to increase at an annual rate of 3.4%. [22] Poverty, lack of education, and unplanned urbanization have increased exposure to CHD risk factors such as: tobacco use, physical inactivity, obesity and unhealthy diets and inadequate nutrition in many urban dwellers. [22]

8. Epidemiology of HIV

The history of HIV begins with the historic 1981 report of Pneumocystis carinii pneumonia (PCP, now attributed to *Pneumocystis jiroveci*) in men who have sex with men, from Los Angeles, USA. [23] In the mid-1980s, HIV and AIDS were virtually unheard of in SSA, yet the region now has the highest burden of HIV and AIDS in the world (Figure 6). [24] SSA countries like Botswana, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Zambia and Zimbabwe have a prevalence of HIV infection of more than 10 %. [25] Fortunately, the incidence of HIV has declined in most SSA countries, with numbers of newly infected patients decreasing by 1/3 to 2/3, though HIV incidence has remained virtually the same in Lesotho and Mozambique. [25] Deaths have declined due in part to antiretroviral treatment (ART) scale-up: 1.2 million people died globally of AIDS in 2014, a 42% decrease since 2004. [25] Unfortunately SSA still remains the epicenter of the HIV pandemic with 70% of the HIV cases. [25] HIV prevalence in Zimbabwe is lowest in the capital Harare Metropolitan Province (13%) and highest in Matabeleland South Province (21%), however there are some hotspots such as resettlements, mines and border towns. All, HIV prevalence is generally slightly higher in urban areas compared to rural areas. [26]

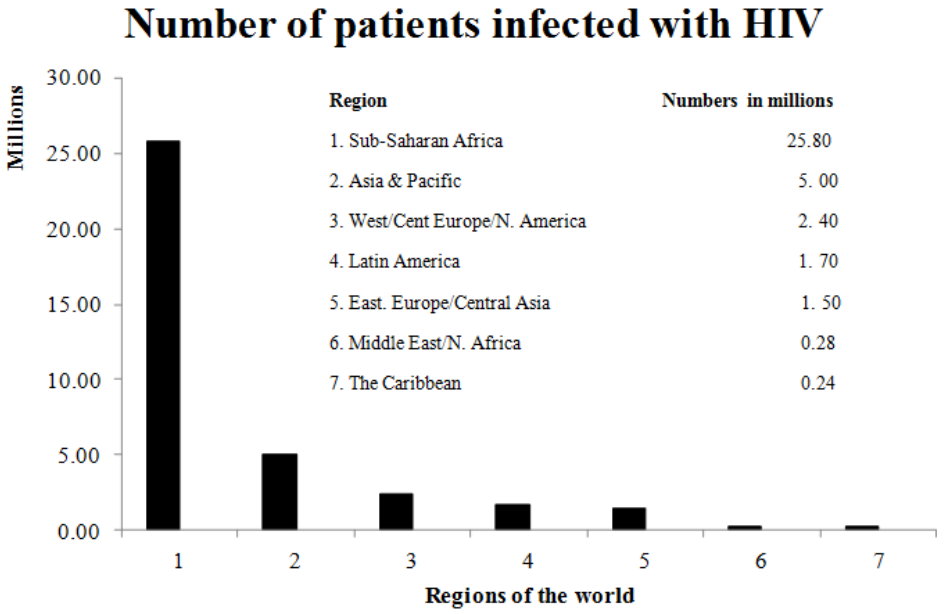

Figure 6. People infected with HIV in different regions of the world (data from 2014 Global HIV Report) [24]

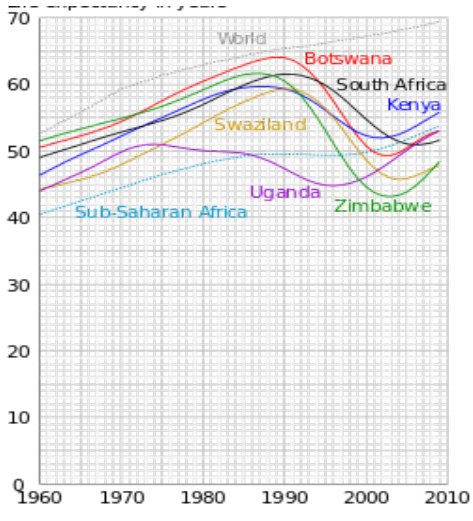

Figure 7. Life expectancy at birth for some Sub-Saharan countries showing the fall from1990s primarily due to the AIDS pandemic [26]

In Zimbabwe the total number of people who died from HIV/AIDS-related illness in 2001 was as high as 200 000. [26] Fortunately, since then AIDS related death rate has decreased from 66,052 in 2012 to 63,853 in 2013 and 39 000 in 2015 due to ART, which, has transformed HIV infection into a manageable disease, and has led to marked improvement in life expectancy for those infected with the virus (Figure 7). [26] Currently, 77% of the HIV infected adults and 55% HIV infected children are on ART. There were 69 000 new infections in 2013, a 34% decline from 2005, with behavior change and high ART coverage thought to be responsible for this decline. [26]

9. Zimbabwe HIV/AIDS Trends

From 1985 when the first AIDS case was reported in Zimbabwe, to the mid-90s, the HIV prevalence rose sharply to reach a peak of 27.7% in 1997 and started

declining thereafter as illustrated in Figure 8. [9] The decline in prevalence is attributed to the impact of prevention programs aimed at behavior change (high condom use and reduction in multiple sexual partners), elimination of mother to child transmission together with successful treatment, care and support services. [9] The rate of new infections, though unreported, was thought to be very high in 2003 with HIV prevalence around 24.6% but decreased to 1.1% in 2013 while the number of people dying from HIV and AIDS related illnesses significantly decreased from a high of 170 000 in 2003 to 60 000 in 2013. [27,28] The epidemic has stabilized because the number of people newly infected with HIV and the number of AIDS-related deaths have declined. [9]

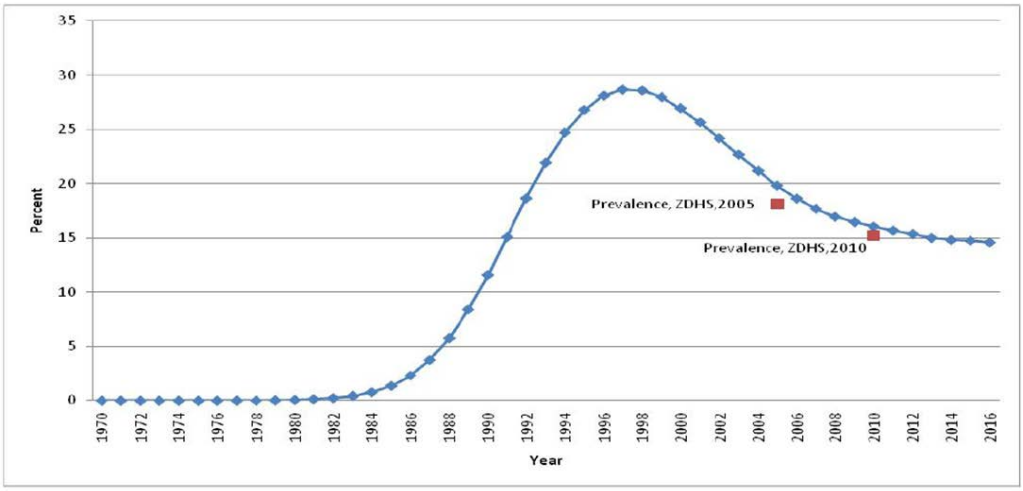

Figure 8. Trends in adult (15-49 years) HIV prevalence in Zimbabwe [9]

10. Antiretroviral Therapy

Globally, ART began with the clinical trial of zidovudine in 1986 and effective combination therapy became available for those living with HIV in rich countries in 1996. ART was so effective that AIDS death rates in developed countries dropped by 84% over 4 years. [29] In 2000, after mounting pressure to make AIDS drugs more accessible, five pharmaceutical companies offered to negotiate steep reductions in the prices of AIDS drugs for Africa and other poor regions. [30] Zimbabwe was a beneficiary, and its national ART program was initiated in April 2004. ART is now an integral part of services for HIV/AIDS prevention, treatment, care, and support. [31] Based on the 2011 Zimbabwe national HIV estimates, it was projected that the number of people in need of ART would increase to 1.4 million in 2016, with the adoption of earlier ART initiation at a higher CD4 threshold of ≤500cells per mL. [31] The Zimbabwe adult ART coverage currently stands at 77% with the percentage steadily increasing especially when the country adopts the new WHO HIV-guidelines in line with American and European guidelines (2015) all of which recommend that all HIV positive patients should be treated with ART. [31]

Globally the number of people with HIV that are receiving treatment has increased to 15.8 million as of June 2015, a 2.2 million increase in one year since June 2014. Those receiving ART (including 823,000 children) - represent 41% of adults in need and 32% of children with HIV. A total of 85% are living in low- and middle-income countries. [32] In light of recent research findings, WHO released a guideline in 2015 recommending starting HIV treatment earlier in the course of illness. [32] Approximately 76% of all people receiving antiretroviral therapy in sub-Saharan Africa are virally suppressed, which means they are likely healthier and less likely to transmit the virus. [32] Globally, the percentage of pregnant women receiving ART for the prevention of mother-to-child transmission of HIV increased to 73% in 2014, up from 36% in 2009; access to ART among children has also risen significantly, although they have less access than adults. [32]

11. Complications of ART

Despite reductions in the incidence of AIDS with effective treatment, in developed countries, patients continue to experience considerable morbidity and mortality from non-AIDS illnesses such as premature CVD, liver failure and renal failure. [11] CVD in HIV-infected patients may be the result of direct cardiac involvement due to opportunistic infectious agents in immune-suppressed patients, HIV-induced immune activation or dyslipidemia and insulin resistance. [33] Indeed although ART decreases HIV/AIDS morbidity and mortality, the long term side effects of the drugs may include the onset of insulin resistance, changes in lipid profile and increased CVD. Dyslipidemia an important adverse effect of ART characterized by alteration of lipid profiles is also caused by HIV per se. [33] Although the underlying mechanisms are not fully understood, HIV infection has been shown to increase the risk of coronary events. Several causative mechanisms have been supposed, including HIV-associated dyslipidemia, endothelial damage or dysfunction, inflammation and hypercoagulability. [33]

12. Global Coronary Heart Disease

CHD is the main cause of CVD and is the leading cause of heart attack and angina in the general l2population in developed countries and has been reported to be increased

in HIV-infected populations as a result of both HIV and antiretroviral therapy (ART). [34] Expanding use of ART not only reduces HIV-associated morbidity and mortality but has been associated with increasing CHD risk, with expected deaths due to CHD projected to double to 2.4 million in 2030 relative to reports from 2000. [34] These data suggest that CHD will become a major health problem in SSA, competing with infectious diseases for limited health resources. [34] Several studies in populations of European descent suggest that HIV infection and ART are independently associated with cardiometabolic diseases including CVD, dyslipidemia and type II diabetes. [34] However, the reports are inconsistent l2and there is evidence to suggest that there may be differences in cardiometabolic disease profiles in people of African descent compared to people of European descent. Such differences may be due to differences in factors such as tobacco usage, alcohol consumption, HIV subtypes and human host genetic factors. [34]

13. Coronary Heart Disease in HIV

Cardiovascular disease (CVD) in HIV infection may be the result of direct cardiac involvement due to opportunistic infectious agents in the presence of advanced immunosuppression, HIV-induced immune activation, or dyslipidaemia and insulin resistance associated with ART. [35] Indeed, although ART decreases HIV/AIDS morbidity and mortality, the long-term side effects of the drugs may include the onset of insulin resistance, changes in the lipid profile and increased cardiovascular risk. [35] The main targets of cardiac disease in untreated HIV infected patients are the pericardium, the myocardium, the coronary arteries and the pulmonary arteries. It seems that ART, by preserving immune function, reduces the incidence of myopericardial disease and pulmonary hypertension. [35]

In developing countries with health systems that cannot guarantee ART to all in need, pericardial disease (often related to tuberculosis), HIV-associated cardiomyopathy and HIV-associated pulmonary hypertension have been reported to be most common cardiac manifestations in HIV. [35] Particularly in SSA, where there is high prevalence of tuberculosis and limited access to ART, pericardial tuberculosis and cardiomyopathy have been thought to be the dominant forms of HIV-associated CVD, while CHD was thought to be the main cause of death and disability in patients from industrialized countries. [35] In contrast to these assumptions, HIV infection known to be an inflammatory disease that results in chronic immune activation and inflammation together with the characteristic dyslipidaemia associated with HIV and its treatment may contribute to increased CHD risk even if the HIV positive patient is from a SSA setting. [35]

14. Conclusion

Zimbabwe demographics, economics and health data are suggestive of a shift in epidemiology of disease with NCD likely to become more important in both the general and HIV infected populations. Fortunately, many NCD can be reduced by applying relevant interventions as has been proven in many high income countries. However, Zimbabwe like many low and middle income countries has a double burden of non-communicable diseases and communicable diseases. Hence despite the drop in HIV prevalence and incidence rate in Zimbabwe HIV/AIDS still retains prime position as the most common cause of death, this in addition to the fact that death rates due to CHD and other non-communicable diseases is continuously rising. There is therefore a need for more attention to be paid to non-communicable diseases like CHD in the Zimbabwean setting to avoid the inevitable collision of CHD and HIV as changing demographics, economics and health conditions have potential to fuel an epidemiologic transition and a likely collision of CHD and HIV in the future.

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