

THE IMPACT OF LIFESTYLE DISEASES ON THE HEALTH CARE SYSTEM IN SUB-SAHARAN AFRICA

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1.0 Abstract

Introduction

Sub Saharan Africa(SSA) is facing a rapidly growing number of people with chronic non-communicable diseases while at the same time experiencing continual high death rates from infectious diseases e.g. HIV/AIDS, TB and malaria. Although this region comprises just over 10% of the world's population, it carries the highest burden of disease in the world. It is well known that some infections increase the risk of certain chronic diseases and vice versa. With an increasing dual burden of disease in SSA, the associations between diseases and our understanding of them will become of increased public health importance. The aim was to explore the relationships reported between HIV, its treatment and metabolic risk.

Methodology

This article is based on review of detailed literature published in MEDLINE and EMBASE since 1997, potentially relevant reports, bulletins and guidelines from the UN, WHO and International Diabetes Federation (IDF).

Findings

Introduction of AntiRetroviral Therapy(ART) in SSA having high prevalence of HIV has been recognized as a public health priority through reduction of its price, raised donor funding and enhanced political commitment e.g. WHO '3 by 5' initiative. This has been associated with an increased risk of developing metabolic syndrome. HIV has been linked with an increased risk of developing both diabetes and cardiovascular disease. Diabetes prevalence and incidence is increasing in SSA compared to the industrialized world due to increased use of ART.

Conclusion

The impact of these co-morbidities in SSA is likely to be large. Roll out of ART coverage within the region is an essential response to the HIV epidemic. However, it is likely to lead to a growing number of individuals suffering from adverse metabolic consequences. HIV disease requires life-long treatment, meticulous adherence to ART and intensive clinical and laboratory monitoring. Therefore, robust and sustainable healthcare systems are needed to provide adequately trained staff, laboratory facilities and a reliable supply of effective drugs with fewer side effects. Research is also needed to develop effective approaches to reducing the frequency and health impact of the co-morbidities described here.

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2.0 Introduction

Lifestyle diseases are those due to the set of habits and customs that are influenced by the lifelong process of socialization, including social use of substances such as alcohol and tobacco, dietary habits, exercise, etc., all of which have important implications for health. (37)

e.g. cardiovascular diseases (CVD's), Diabetes Mellitus (DM) type 2, chronic respiratory disease, cancers, etc. These chronic diseases are the leading cause of mortality worldwide (60% of all deaths), and 80% of these deaths occur in developing countries. In Sub-Saharan Africa (SSA), infectious diseases still cause the majority of mortalities (69% of deaths) while chronic non-communicable diseases contribute around a quarter of deaths (47). This picture is changing as SSA undergoes an epidemiological transition with a rapidly increasing burden of, and associated mortality from, chronic non-communicable diseases.

“Cancer, diabetes, heart diseases are no longer diseases of the wealthy. Today, they hamper the people and economies of the poorest populations, even more than infectious diseases. This presents a public health emergence in slow motion”, said Hon. Mr. Ban Ki-Moon, UN Secretary-General.

3.0 Objectives

4.1 Broad objective: To explore the relationships reported between HIV, its treatment and metabolic risk.

4.2 Specific objectives: 1. To review the current status of HIV/AIDS in SSA and the African continent at large. 2. To explore how HIV and ART predispose to lifestyle diseases like Type 2 diabetes and cardiovascular disorders by causing the *metabolic syndrome*.

5.0 Methodology

This article is based on review of detailed literature published in MEDLINE and EMBASE since 1997, potentially relevant reports, bulletins and guidelines from UN, WHO and International Diabetes Federation (IDF).

6.0 Findings

6.1 HIV/AIDS in Sub Saharan Africa (SSA)

SSA is more heavily affected by HIV/AIDS than any other region of the world. It is estimated that 67% (22.4 million) of all people infected with HIV worldwide resided in SSA and that the majority (72%) of deaths globally occurred here (2.8 million deaths). In 2008, an estimated 1.9 million people became newly infected with HIV and around 1.4 million people died from AIDS in SSA representing an 18% decline in annual HIV-related mortality in the region since 2004. Since the beginning of the epidemic, more than 14.1 million children have lost one or both parents due to HIV/AIDS (1).

All Southern African countries with the exception of Angola have an estimated adult HIV prevalence above 10%. In three southern African countries, the national adult HIV prevalence rate now exceeds 20%. These countries are Botswana (23.9%), Lesotho (23.2%) and Swaziland (26.1%). Adult HIV prevalence in East Africa exceeds 5% in Uganda, Kenya and Tanzania (5, 2007 AIDS Epidemic Update).

6.2 HIV and ART causing Metabolic Syndrome (MS)

The range of potential adverse consequences of ART is wide and includes gastro-intestinal disturbance, hepatotoxicity, pancreatitis, peripheral neuropathy, mitochondrial toxicity, anaemia, dyslipidaemia, insensitivity to insulin, and the excessive loss of fat beneath the skin (lipoatrophy) – resulting in sunken cheeks, indentations, and hollow eyes (29, 32). Risk associations between HIV, its treatment, and various features of metabolic syndrome have been

reported. It's during the treatment of HIV with ART that metabolic syndrome (MS) can be induced.

The following describes the association between HIV and three major components of MS i.e., dyslipidaemia, lipodystrophy and insulin resistance separately;

6.3 Risk of HIV Lipodystrophy (HIV-LD) in HIV⁺ patients

HIV-LD is seen in long term survivors of HIV infection, most of whom are receiving ART. HIV-LD is a complex syndrome thought to occur due to the secondary effects of HIV infection, direct drug-induced toxicities and/ or the indirect effects of changes in body composition on lipid metabolism (19). The syndrome consists of both metabolic abnormalities (hyperlipidaemia and IR) and body fat redistribution (central adiposity and peripheral fat wasting). Central adiposity is manifested by the accumulation of visceral fat in the intra-abdominal space (abdominal obesity), dorsocervical spine (buffalo hump) and the breasts. Peripheral wasting describes loss of subcutaneous adipose tissue (lipoatrophy) in the limbs, face and buttocks in a generalised fashion. (16).

The risk of central adiposity and peripheral wasting is greatly increased in HIV⁺ patients on ART. In the Lancet in 1997, the first report on body fat redistribution in an HIV⁺ person associated with PI-treatment was published (24). The following year, 1998, Carr *et al* designed a cross-sectional study to characterize the syndrome that was leading to this observed body fat redistribution and to determine if it was seen in association with all protease inhibitor (PI) use or only in HIV patients using PI's. Healthy individuals, PI naïve HIV⁺ patients and HIV⁺ patients on PI's, were compared (10).

It was already known that PI's cause certain metabolic abnormalities such as hyperglycaemia but this publication was the first to report that HIV patients on PI's had an increased risk of developing a syndrome of lipodystrophy with hyperlipidaemia and IR. It is now accepted that PI and other ART use in HIV⁺ individuals are associated with fat redistribution.

Studies on nevirapine (6) (an NNRTI), stavudine and lamivudine (29, 33) (NRTIs) have all shown an association between usage and changes in fat deposition. All ART trials that have included objective body shape evaluation have consistently found an increased risk of abdominal fat in HIV patients regardless of which ART is used. However it is unknown which ART's cause the most severe accumulation of visceral fat (17).

Stavudine (especially in combination with didanosine) and to a lesser extent zidovudine are associated with higher risk of lipoatrophy (9)

6.4 Risk of Dyslipidemia in HIV⁺ patients

Dyslipidaemia is characterised by hypertriglyceridaemia, hypercholesterolaemia and low serum HDL cholesterol, features of defective lipoprotein metabolism (11). Although abnormal lipid profiles are reported in HIV⁺ individuals before the use of ART, hypertriglyceridaemia becomes more prevalent and severe during treatment (17). Sullivan *et al* in 1998 reported a case in which serum triglycerides markedly increased after 5 months of treatment with ritonavir (a PI). In the same patient there was also an increase in cholesterol. Both concentrations returned to baseline 5 weeks after discontinuing ritonavir hence showing the association to be treatment rather than infection led (38).

Hypertriglyceridaemia and hypercholesterolaemia have been reported to occur with long term usage of drugs from the three main classes of ART; however, the association seems most common place with the use of PI's. Chen *et al* report prevalence of dyslipidaemia (defined as hypertriglyceridaemia, hypercholesterolaemia and low HDL) in HIV⁺ individuals being treated with HAART as 70-80% and state that it can be associated with all available PIs (11). It has also been reported that severe hypertriglyceridaemia associated with PI therapy can lead to

acute pancreatitis (38).

PIs and NRTIs are associated with insulin resistance and hyperglycaemia. Of all PIs, atazanavir and darunavir are less likely to cause dyslipidaemia while saquinavir and atazanavir are less likely to impair glucose tolerance (9).

6.5 Risk of Insulin Resistance (IR) in HIV⁺ patients

It is also known that HIV⁺ people are at increased risk of IR due to the pro-inflammatory process of HIV, the direct effects of ARTs and also, indirect effects as consequences of ART (for example body fat distribution changes). The pathogenesis of ART-induced IR has been the focus of much discussion. Evidence suggests that body fat distribution changes cause increased fat deposition in muscle which is accompanied by impaired insulin sensitivity (2). It has been shown that ART regimens impair glucose tolerance in one of two ways; induction of peripheral IR in skeletal muscle and adipose tissue and impairment of pancreatic beta cells' ability to compensate (2). It has also been reported that PI's bind to and block the insulin sensitive glucose transporter GLUT4 (21).

Less is known about the mechanisms involved in the effect of NRTI's on insulin sensitivity (35). It has been well documented that IR is related to abdominal obesity, hypertriglyceridaemia and is associated with type 2 DM (10). There is much controversy as to whether it is changes in body composition that reflect underlying metabolic changes or vice versa (48). In a recently published study in which ART-naïve patients were randomised to receive either an NRTI-regimen or an NRTI-sparing regimen, glucose and insulin were assessed before and approximately three months after initiation of therapy. The researchers reported that there was a reduction in peripheral insulin sensitivity without significant changes in body fat distribution in the NRTI group but not the NRTI-sparing group (8). These findings indicate that the changes are not mediated by alteration in body composition but that the risk is associated with NRTI usage.

6.6 Risk of Heart Disease in HIV⁺ patients

Magula and Mayosi (2003) looked at cardiac involvement in HIV patients and showed that abnormalities are commoner in HIV patients. Approximately half of hospitalized HIV patients and a high number of out-patients were found to develop cardiac abnormalities (28). The DAD study (Data collection on Adverse events of anti-HIV Drugs) assessed the risk of Myocardial Infarction (MI) in HIV patients by measuring the incidence of MI in terms of duration of HAART. The relative risk of an MI for an HIV patient on HAART was shown to be raised and to increase over time (15). In another study, cardiovascular disease risk was found to be significantly higher in HIV patients with MS in comparison to HIV patients with only abnormal body fat redistribution. This shows that MS increases the risk of MI more severely than body fat changes alone. Based on the Framingham criteria (27) the researchers report median percentage of cardiovascular disease risk at ten years for those with the MS and those without to be 10 and 5 respectively. It is not known how the traditional cardiovascular risk factors (e.g. smoking) modulate risk in the HIV population (17). Currently, osteonecrosis has been reported in patients with advanced HIV disease or following long exposure to combination of ART but more research is needed to clarify this (9).

7.0 Discussion

Importance of these associations in a SSA setting

Although much research is needed before we fully understand the biological pathways and effect on disease rates of the associations between the chronic and infectious diseases discussed in this paper, it is clear that they could potentially have a large public health impact within SSA.

Effective treatment of HIV infection with ART in Africa is now available even in countries with limited resources and the number of individuals receiving treatment has been greatly increased by the 3' by 5' campaign and 'All by 2010' (2007 AIDS Epidemic Update). The large increase that has occurred in the number of people on ART has meant the number of people living with AIDS as a chronic condition has massively increased.

The WHO and UNAIDS 3' by 5' initiative is aimed at providing treatment to 3 million people in low and middle income countries by 2005. By December 2005, 18 countries had met their 3' by 5' target and 1.3 million individuals were receiving ART. In SSA, the number of people receiving HIV treatment increased more than eight-fold to 810,000 from 100,000. Despite these increases in ART, only 20% of those in need of treatment were receiving it by December 2005. The G8 nations and the UN national assembly agreed to work with WHO and UNAIDS to continue developing an essential package of HIV prevention, treatment and care with the aim of moving as close as possible to universal access to treatment by 2010.

The 'All by 2010' target is also part of MDG 6 which includes the goal of halting and beginning to reverse the spread of HIV/AIDS by 2015. The treatment of HIV with ARTs is a huge and greatly needed advance decreasing morbidity and mortality from HIV substantially but it has some unintended consequences that require either preventive efforts or appropriate treatment. If the goal of universal ART treatment within SSA is met then a substantial rise in metabolic syndrome, diabetes and heart disease may be seen. More research is needed to know how important this relationship will be globally and within SSA.

8.0 Conclusion

SSA is currently seeing a very large change in the major health problems it faces. The link between chronic and infectious diseases becomes more important as the epidemiological transition in SSA progresses against a backdrop of globalization. Although associations between HIV, its treatment using ART and HIV-LD, insulin resistance, dyslipidemia and heart disease are now accepted as occurring in western environments, the mechanisms through which these occur are still under debate. More research is needed in low income countries in order to find the extent to which these issues will be a problem in SSA.

9.0 Recommendations

The need for an effective health chain

However, in SSA the healthcare infrastructure is underdeveloped, and suffers from lack of adequately trained professionals, insufficient support for adherence to treatment, and interruptions in drug supply. It is a sad fact that while SSA carries over 60% of the global burden of disease, it spends less than 1% of the total global health expenditure. In this regard, innovative healthcare delivery and financing models will be needed to ensure appropriate and sustained management of chronic diseases. Tackling the HIV/AIDS crisis in Africa is a long-term task that requires sustained effort and planning - both within African countries themselves and within the international community. One of the most important elements of the fight against AIDS is the prevention of new HIV infections. HIV prevention campaigns that have been successful within African countries need to be highlighted and repeated.

The other main challenge is providing treatment and care, in particular ARVs, which can allow people living with HIV to live longer and healthier lives. Many African countries have made significant progress in their treatment programmes in recent years and it is likely that the next few years will see many more people receiving the drugs. However, more research is needed in order to innovate effective ARV drugs with fewer long-life side effects or if possible the

vaccine for this tragedy.

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**THE BEST WAY TO CONTROL HIV/AIDS
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