Metabolic clinic for individuals with HIV/AIDS: a commitment and vision to the future of HIV services

Mohamed H. Ahmed[a], Clare Woodward[b] and Dushyant Mital[b]

One of the biggest current challenges in managing an ageing cohort living with the HIV is handling dyslipidaemia, diabetes, metabolic syndrome and nonalcoholic fatty liver disease. Combination antiretroviral therapy decrease mortality and morbidity in HIV patients, but lead to increase in insulin resistance, dyslipidaemia, abnormalities of fat distribution and high risk of cardiovascular disease. Therefore, a metabolic clinic was established for individuals living with HIV in the Milton Keynes University Hospital NHS Foundation Trust. The clinic meets considerable demands by service users and hence has the potential to be popular. This review focuses on the importance of the development of a metabolic clinic for the purpose of audit, research, teaching and exchange of knowledge between HIV specialists and the metabolic team in the management of complex cases. Therefore, the metabolic clinic should be an integral part of HIV services especially as the cohort of the 'older' HIV population increases. *Cardiovasc Endocrinol* 6:109–112 Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.

Departments of [a]Medicine and HIV Metabolic Clinic and [b]HIV and Genitourinary Medicine, Milton Keynes University Hospital, NHS Foundation Trust, Milton Keynes, UK

Correspondence to Mohamed H. Ahmed, MD, PhD, Department of Medicine and HIV Metabolic Clinic, Milton Keynes Hospital NHS Foundation Trust, Eaglestone, Milton Keynes, Buckinghamshire MK6 5LD, UK
Tel/fax +44 1908 86363; e-mail: elziber@yahoo.com

Introduction

HIV per se can lead to diabetes, dyslipidaemia and nonalcoholic fatty liver disease (NAFLD); therefore, it is not surprising that HIV showed an independent effect on cardiovascular risk [1–3]. Each of these metabolic factors was also reported with the administration of combination antiretroviral therapy (cART) [2,4,5]. For instance, dyslipidaemia is reported in around 82.3% of HIV patients receiving antiretroviral medication [6]. Furthermore, in addition to dyslipidaemia, the cART medication in HIV patients is associated with an increase in the prevalence of insulin resistance and diabetes [6–8]. The increase in the ageing population of HIV patients may also lead to an increase in the incidence of cardiovascular disease (CVD). The prevalence of CVD was found to be around 23% in elderly individuals with HIV [5]. It is well recognized that HIV is a multisystem disorder and this may significantly lead to an increase in mortality. One study showed an increased percentage of death attributable to cardiac, renal and hepatic disease among HIV patients treated with cART [5]. The aim of this article is to review the challenges of obesity, dyslipidaemia, diabetes and NAFLD in HIV patients and the potential benefits of metabolic clinic as an integral part of HIV services.

Diabetes mellitus, metabolic syndrome and HIV

Several studies from Africa, the Far East and South America showed an increase in the prevalence of insulin resistance and diabetes in particular with cART [9–13]. In one study, the prevalence of diabetes mellitus was 2.1% [14]. The prevalence of diabetes in Western HIV populations ranges from 2.6 to 14% in those with treated HIV in various cohort studies [15]. Importantly, pre-existing hypertension, obesity and diabetes increased the risk of dyslipidaemia or the changes in body configuration associated with cART such as central obesity, truncal obesity and lipoatrophy, and these may all increase the risk of diabetes mellitus [16]. This is likely because of the fact that HIV represents a chronic inflammatory condition and this may lead to both dyslipidaemia and insulin resistance [17]. HIV and cART medication may impair lipid metabolism and increase triglycerides and the risk of insulin resistance. Furthermore, increased oxidative stress, impaired function of adipokines and transcript factors (adiponectin, leptin, sterol regulatory-binding proteins and peroxisomal proliferatory activator receptors α and γ lipoatrophy and lipohypertrophy) may also lead to insulin resistance and diabetes [7,18–20]. Importantly, protease inhibitors (PIs) are not only associated with dyslipidaemia because of mitochondrial toxicity but also hyperglycaemia because of inhibition of glucose transporter type 4, and this leads to inhibition of adipocyte differentiation and an increase in triglyceride levels and insulin resistance [21]. Furthermore, treatment with PI and nucleoside reverse-transcriptase inhibitor (NRTI)-containing regimens was associated with the risk of development of type 2 diabetes mellitus [22].

Dyslipidaemia in HIV patients

High cholesterol and triglycerides and low high-density lipoprotein (HDL) are common features of HIV dyslipidaemia [18]. Common medications used in the treatment of HIV are PIs, NRTIs and non-NRTIs [23], and these can also precipitate dyslipidaemia. For instance, administration of cART is associated with decreased HDL-c, increased very low-density lipoprotein (LDL) and increased total cholesterol. PI-based regimes are associated with incidences of dyslipidaemia in 70 and 80% of patients in the form of high triglycerides, LDL and decreased HDL-c and accumulation of Apo-E and Apo-C III [24]. PIs are also associated with central obesity, lipoatrophy and insulin resistance [25]. The PIs mediate this effect through inhibition of lipogenesis, adipocyte differentiation and decrease in the hepatocyte clearance of hepatic chyliomicron and very LDL and stimulation of hepatic synthesis of triglycerides [24]. Other medications such as NRTIs are also associated with high triglycerides and lipoatrophy, apart from tenofovir, which appears to be a good choice when dyslipidaemia is an issue with the administration of NRTIs [25]. Furthermore, NRTIs such as abacavir and didanosine are associated with an independent risk of myocardial infarction in the Data Collection on Adverse Events of Anti-HIV Drug (DAD) study [4], whereas nevirapine protected against low HDL-c level and efavirenz is associated with an increase in total cholesterol and triglycerides [26]. Pravastatin, atorvastatin and rousvastatin are good choices in the treatment of HIV dyslipidaemia.

Nonalcoholic fatty liver disease and HIV

The presence of insulin resistance, dyslipidaemia and lipoatrophy are all precursor factors that lead to the development of NAFLD, which refers to a wide spectrum of liver damage, ranging from simple steatosis to steatohepatitis, advanced fibrosis and cirrhosis [27]. The estimated prevalence of NAFLD in a population without HIV is believed to be around 25–35% worldwide [28]. The prevalence of NAFLD in Asian patients with HIV is estimated to be around 31% and was associated with high BMI, dyslipidaemia and a high alanine aminotransferase/ aspartate aminotransferase ratio [29]. In a population-based study, the prevalence of NAFLD was found to be around 26% and associated with an increase in γ-glutamyl transpeptidase and insulin resistance [30]. Importantly, HIV patients with hepatitis C can also have NAFLD [31, 32]. Furthermore, NAFLD gained significant scientific attention because of the fact that it is considered a common and fast-growing liver disease worldwide, with an increase in both mortality and morbidity [28]. The association between NAFLD and HIV and antiretroviral treatment has been reported in several studies [33–35]. This is likely because of the association of NAFLD with insulin resistance and the high risk of CVD and dyslipidaemia [26,27]. NAFLD is common in HIV patients and is associated with greater visceral adiposity and insulin resistance [36]. The only effective therapy for NAFLD is weight loss and the use of statin with NAFLD appears to be safe and effective.

Cardiovascular risk and HIV disease

The increase in the risk of CVD in HIV patients was shown in several studies. In the DAD study [4] that investigated the impact of diabetes and pre-existing coronary heart disease (CHD) on the development of a new CHD episode among 33 347 HIV-infected individuals, it was shown that the rate of a CHD episode was 7.52 times higher in those with pre-existing CHD than in those without pre-existing CHD, but it was only 2.41 times higher in those with pre-existing diabetes mellitus compared with those without diabetes mellitus [37]. The DAD study also showed that the prevalence of metabolic syndrome increased from 19.4 to 41.6% within 6 years [38]. Triant *et al.* [39] showed that HIV is associated with an increased incidence of acute myocardial infarction in HIV patients in comparison with non-HIV patients, and this is likely because of the higher prevalence of hypertension, diabetes and dyslipidaemia in the HIV cohort. Importantly, PIs are also associated with a higher risk of incidence of myocardial infarction and this in part because of dyslipidaemia [40]. Because of the fact that individuals with HIV live longer, an increase in comorbidities such as diabetes, dyslipidaemia, chronic kidney disease, hypertension and CVD was noted [14]. It is plausible to suggest that this will lead to a significant burden on health resources in the near future unless correct strategies are planned carefully. Therefore, we have established the metabolic clinic as part of the integral HIV services in Milton Keynes University Hospital and it is one of the leading metabolic clinics for HIV patients in UK.

Why is it important to establish metabolic clinics for HIV patients?

The metabolic clinic in Milton Keynes University Hospital is a weekly clinic that runs within the HIV clinic. Patients see a specialist in metabolic medicine and a dietician. A thirty minute meeting before the beginning of the clinic is allocated for discussion of cases between the metabolic team and HIV consultants. At present, this is not a referral clinic, but is part of the future expansion of the services. It is funded by the National Health Service and the system is currently sustainable. The 'inclusion criteria' for entry into the metabolic clinic are as follows:

(1) over weight and obesity,
(2) underweight,
(3) hypertension,
(4) dyslipidaemia,
(5) diabetes,
(6) nonalcoholic fatty liver disease,
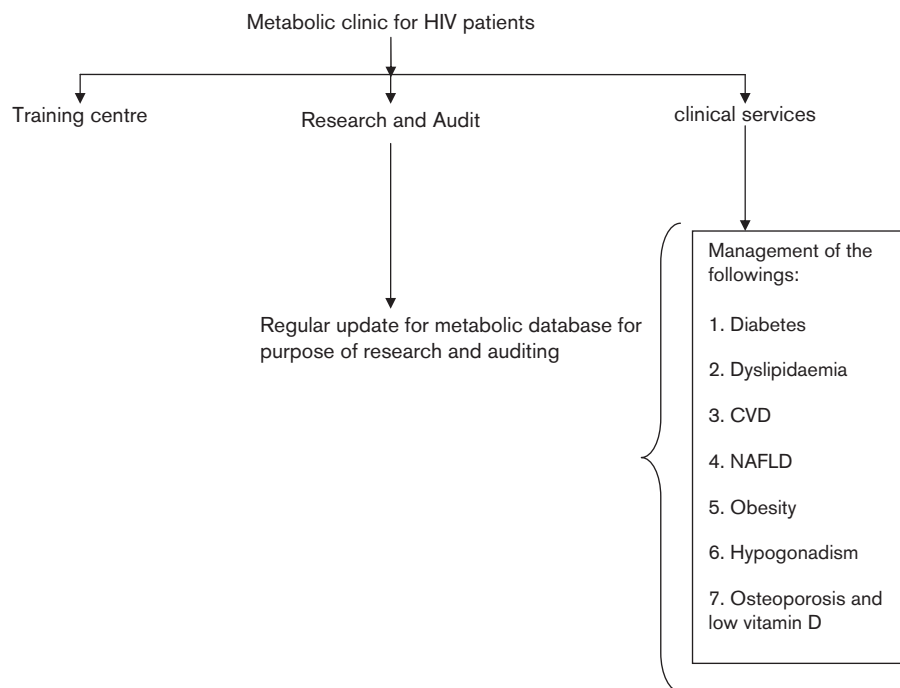(7) hypogonadism and low testosterone,

Fig. 1

Illustration of the different roles of metabolic clinic for HIV patients. CVD, cardiovascular disease, NAFLD, nonalcoholic fatty liver disease.

(8) other endocrine disorders such as (high calcium, thyroid dysfunction).

Recently, a cardiology clinic was established for HIV patients in London [41]. It is possible to suggest that a more specialist input (nephrology, neurology and oncology) will be a part of the HIV services. Several factors can be counted for why it is important to establish a metabolic clinic:

(1) Running a metabolic clinic within the same HIV department makes patients feel more comfortable with the same staff who care for their HIV management in a seamless way.
(2) A metabolic clinic reviews HIV patients with dyslipidaemia, type 2 diabetes, metabolic syndrome and obesity, NAFLD, hypogonadism and impotence, and we also recommend treatment for HIV patients with definitive cardiovascular risk factors (Fig. 1). As the clinic is relatively new (2 years old), we are in the process of establishing a guideline for patients with multimorbidity.
(3) A metabolic database is available for the purpose of auditing, research and teaching.
(4) The clinic provides a platform for exchange of ideas and knowledge between HIV specialists and the metabolic team, especially for the management of complex dyslipidaemia and CVD. The infectious disease physician is also a part of the multidisciplinary team meeting team in managing HIV and medications as part of the metabolic disease.

Conclusion
HIV patients live longer and encounter a series of challenging metabolic disorders such as diabetes, obesity, dyslipidaemia, NAFLD, vitamin D deficiency and increased risk of CVD. The dyslipidaemia can be because of HIV infection or may be induced by HIV medication. The metabolic clinic will not only meet the clinical demand for clinical services but also provide a useful opportunity to collect data for future clinical research and auditing. In view of the fact that we will soon face the challenge of an ageing population of HIV patients, the metabolic clinic could also be used to train future HIV physicians/metabolic medicine physicians/endocrinologists and elderly care physicians in the management of these complex metabolic disorders (Fig. 1).

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