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Review Article

Metabolic syndrome in HIV-positive patients

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ABSTRACT

A number of abnormalities related to chronic infection and antiretroviral treatment may be observed in a population of HIV-positive patients. A particular state of coexisting, interacting and interrelated disorders referred to as metabolic syndrome is observed in 7–45% of patients infected with HIV. Its presence is related to the abnormalities of adipose tissue distribution known under a common name of ART-related lipodystrophy syndrome. The most common features of metabolic syndrome observed in a course of HIV infection include hypertriglyceridemia and low HDL cholesterol concentration, while increased waist circumference is the least frequently observed. Treatment of metabolic syndrome encompasses revision and possible changes in antiretroviral therapy, diet, changes in physical activity, pharmacological management of individual components of the syndrome. In this publication we present a review of problems concerning epidemiology, pathophysiology, symptoms and treatment of metabolic syndrome in HIV-positive patients.

1. Introduction

The term "metabolic syndrome" (MS) refers to a particular condition where coexisting, interrelated metabolic disturbances interact, significantly increasing the risk of developing atherosclerosis, cardiovascular disease and type 2 diabetes [1]. Creation of the definition also known as "syndrome X" is attributed to Gerald Raven, who introduced a description of cluster occurrence of such disorders as: dyslipidemia, impaired glucose tolerance and hypertension, and considered all of these disturbances independent risk factors of cardiovascular disease [1]. Gradually increasing knowledge about these disorders led to development of the concept of insulin resistance and, ultimately, metabolic syndrome. The most important etiopathogenetic factor of MS is resistance to insulin action and hyperinsulinemia. Disorders comprising MS include: abdominal obesity, dyslipidemia, elevated triglyceride (TG) levels, reduced HDL cholesterol concentration, hypertension and impaired glucose tolerance or diabetes. Moreover, hypercoagulability (disorders of coagulation and fibrinolysis) and proinflammatory states (laboratory markers of inflammation) are more frequently observed in MS patients. Among many previously established definitions, the following classifications are most widespread, due to their applicability, and considered most valid: National Cholesterol Education Program – Adult Treatment Panel III (NCEP ATP III) and International Diabetes Federation (IDF). Both classifications are presented in Table 1 [2–4].

Diagnosis of MS is important with regard to identification of individuals with increased risk of cardiovascular disease and diabetes, as well as implementation of multidirectional management aimed at prevention and treatment of complications related to this syndrome. According to the 2005 WOBASZ study, MS affects 22.8% of men and 20% of women in Poland and its prevalence increases with age [5].

2. Prevalence of metabolic syndrome among HIV-positive patients

Widespread application of highly active antiretroviral therapy (HAART)/combination antiretroviral therapy (cART) significantly reduced the morbidity and mortality associated with AIDS. Survival of HIV-infected patients significantly increased with simultaneous increase in the incidence of related diseases and disorders, including metabolic syndrome. Classical risk factors for cardiovascular disease (CVD), such as: age, sex, dyslipidemia, hypertension, type 2 diabetes and habits related to lifestyle – smoking, improper diet,

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Table 1
NCEP ATP III and IDF criteria for the diagnosis of metabolic syndrome [2–4].

NCEP/ATP III definition – 2004		IDF definition – 2005	
Risk factor	Level	Risk factor	Level
3 or more coexisting factors		Prerequisite for diagnosis	
Abdominal obesity/waist circumference	Men > 102 cm Women > 88 cm	Abdominal obesity/waist circumference[a,b]	Men ≥ 94 cm Women ≥ 80 cm
Triglycerides	≥150 mg/dL or specific treatment for hypertriglyceridemia	and at least 2 of 4 factors: Triglycerides	≥150 mg/dL or specific treatment for hypertriglyceridemia
HDL-cholesterol	Men < 40 mg/dL Women < 50 mg/dL or specific treatment for dyslipidemia	HDL-cholesterol	Men < 40 mg/dL Women < 50 mg/dL or specific treatment for dyslipidemia
Blood pressure	sBP ≥130 or dBP ≥85 mmHg or specific treatment for hypertension	Blood pressure	sBP ≥130 or dBP ≥85 mmHg or specific treatment for hypertension
Fasting glucose	≥100 mg/dL or specific treatment for hyperglycemia	Fasting glucose	≥100 mg/dL or previously diagnosed type 2 diabetes

[a] IDF definition takes into consideration differences and sets norms for races and ethnic groups with respect to waist circumference. The above criteria are defined for Europeans [4].
[b] If BMI is >30, central obesity can be assumed [4].

lack of physical activity, are present in a population of patients with HIV. However, unlike general population, HIV patients are exposed to specific, non-classical CVD risk factors associated with the infection and its treatment. Those risk factors include metabolic disorders induced by combination of antiretroviral therapy and inflammation related to chronic infection [6,7]. Frequency of occurrence of MS among HIV-positive patients is estimated at 7–45% depending on the design of the study, assumptions and classifications used (Table 2) [7–16].

3. Pathophysiology of metabolic syndrome related to antiretroviral therapy

Due to widespread application of ART, including the necessity of protracted use of a variety of drugs with different mechanisms of action, the matter of drug interactions and adverse reactions became very important. A number of studies indicate the association between occurrence of MS and use of HAART, particularly with protease inhibitors (PIs), although there are also studies that contradict the above observations. In a study by Jerico et al. and Samaras et al. the occurrence of MS was associated with current exposure to PI [10,12]. Jacobson et al. pointed to the relationship between MS and treatment with lopinavir/ritonavir or didanosine [16]. On the other hand, in a prospective 3-year-long study symptoms of MS occurred with similar frequency among treated and untreated individuals, although there were differences with regard to syndrome quality [17]. Other studies have not shown significant differences in the incidence of MS between patients treated and untreated with HAART, or influence of HAART on MS either [18–20].

Table 2
Incidence of metabolic syndrome among HIV-positive patients according to various authors [7–16].

	Incidence of MS	Classification of MS	Mean age	Study group	Proportion of men (%)
Gazzarusso 2002	45.50%	NCEP	37	553	66
Jerico 2005	17%	NCEP	42	710	80
Estrada 2006	15.80%	NCEP	41	146	66
Bergersen 2006	15%	NCEP	42	357	80
Mondy 2006	25.50%	NCEP	43	471	66
Baum 2006	15.10%	NCEP	42	118	74
Jacobson 2006	24%	NCEP	45	477	75
Palacios 2007	16.60%	NCEP	41	60	83
Bonfanti 2007	20.80%	NCEP	43	1263	50
	22.10%	IDF			
Samaras 2007	18%	NCEP	41	788	84
	14%	IDF			
Wand 2007	8.50%	NCEP	38	881	80
	7%	IDF			
Falasca 2007	42%	NCEP	74	54	41
Mangili 2007	22.90%	NCEP	45	314	64
Sobie 2008	33%	NCEP	42	36	0
Adeyemi 2008	34%	NCEP	54	121	79
Saint Martin 2008	7.1%	NCEP	41	140	72
Hansen 2009	27%	NCEP	44	566	80
Worm 2009	19.40%	NCEP	38	23 202	74
Jevtovic 2009	29.10%	NCEP	44	399	69
Bonfanti 2010	12.30%	NCEP	37	357	75
Avotedu 2010	26.6%	NCEP	37	321	13
	22.7%	IDF			
Kwiatkowska 2011	26.3%	NCEP	39	72	67
	34.7%	IDF			
Yuhana 2012	32.5%	NCEP	42.5	126	