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ScienceDirect
Metabolism Clinical and Experimental 56 (2007) 135–141
Metabolism
Clinical and Experimental
www.elsevier.com/locate/metabol

Metabolic syndrome prevalence and characteristics in Greek adults with familial combined hyperlipidemia☆

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Received 3 February 2006; accepted 18 September 2006

Abstract

Familial combined hyperlipidemia (FCH) is closely related with metabolic syndrome (MetSyn), and coronary artery disease (CAD) is positively associated to MetSyn and FCH. In this study, we evaluated the prevalence of MetSyn and its components between patients with FCH and a control group. We also investigated the role of MetSyn and diabetes mellitus (DM) on the incidence of CAD within the FCH group. Our study population consisted of 463 male and 243 female patients with FCH who were not receiving any hypolipidemic treatment, and 1128 men and 1154 women who came from the same geographical region. The prevalence of MetSyn was 42% and 19.8% among FCH subjects and controls, respectively, whereas MetSyn increased with age in both groups. The prevalence of CAD was 15.3% in the FCH group. Moreover, after dividing FCH patients into 3 subgroups, with and without MetSyn and with DM, CAD prevailed at a percentage of 15.2%, 11.1%, and 26.5%, respectively. However, statistically significant differences in the prevalence of CAD were observed only between FCH subjects with DM compared with the other 2 subgroups, even when an adjustment for age, sex, and smoking was conducted. People with FCH and MetSyn differed in several anthropometric, biochemical, and clinical characteristics, compared with the non-MetSyn subgroup of FCH. MetSyn is more prevalent in the FCH than in the control group. Among subjects with FCH, only DM was significantly associated with an increase in the prevalence of CAD in this subgroup compared with FCH individuals with or without MetSyn.
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1. Introduction

Metabolic syndrome (MetSyn), a clustering of abdominal obesity, dyslipidemia, hypertension, insulin resistance, and disturbed glucose metabolism, is a growing health issue that strongly correlates with the increased burden of cardiovascular disease and of diabetes mellitus (DM) [1]. The Third National Health and Nutrition Survey has estimated that 1 of 5 US citizens have this condition [2], a statement that is in agreement with the results from the ATTICA study in a representative sample from the general population in Greece [3]. Metabolic syndrome is presented as a polygenic and multifactorial disorder. The lipidemic profile of this condition, which consists of increased levels of triglycerides, apolipoprotein B (apo B), small, dense low-density lipoproteins (LDL), and of small amounts of high-density lipoproteins (HDL), seems to be the cornerstone of its atherogenic power [4]. Thus, the Adult Treatment Panel III (ATP-III) described MetSyn as a secondary target of the risk-reduction therapy according to the levels of LDL cholesterol (LDL-C) [1]. Furthermore, the profile of MetSyn can be attributed to central obesity and the consequent insulin resistance through various pathophysiologic mechanisms [5-9].

However, the same metabolic abnormalities also characterize familial combined hyperlipidemia (FCH) and type 2 DM [10-12]. FCH is the most common inherited polygenic disorder that affects 1% to 2% of the general population and is associated with a 2- to 3-fold increased risk of coronary artery disease (CAD) [13,14], especially in younger ages.

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doi:10.1016/j.metabol.2006.09.007

The conventional wisdom is that the 2 conditions etiologically overlap; however, only Hopkins et al [15] explored differences in the prevalence of MetSyn between subjects with FCH and controls.

The aim of this work was to compare the epidemiology of MetSyn between people with FCH and a population-based sample of Greek adults, both from the prefecture of Attica, and to investigate the association of MetSyn and DM with the prevalence of CAD in the FCH group.

2. Methods

2.1. Study population

In this study, 706 patients with FCH (463 men and 243 women) were enrolled; they had been referred, for the first time to our lipid outpatient clinic during 1999-2003. Moreover, data regarding 1128 men and 1154 women with FCH (who participated in the ATTICA study) from the general population of the same geographic region were retrieved [3]. The sampling of the ATTICA study was random and multistage (by city) and was based on the age and sex distribution of the province of Attica provided by the National Statistical Service according to the census of 2000.

All subjects were Caucasian and lived in the prefecture of Attica in Greece. On admission to the lipidemic outpatient clinic, the patients with FCH were not under any hypolipidemic treatment (lifestyle interventions, drug therapy). A complete medical history was obtained from all the participants, and a physical examination was performed.

The well-known phenotypic variability of FCH leads to a lack of consensus about the diagnostic criteria. There have been several patterns suggested, but we decided to use the following as diagnostic criteria for FCH: (1) plasma levels of total cholesterol (TC) and triglyceride (TG) concentration greater than 90th percentile, as determined by using the age- and sex-related 90th percentile upper levels of the Prospective Cardiovascular Munster study, which was confirmed by at least 2 repeated measurements with a minimum interval of 2 months; (2) the presence of type II-a, II-b, or IV hyperlipidemia in at least one first-degree relative and familial history of early atherosclerotic disease, which are adopted in most of the relative studies [13,14,16].

The MetSyn was defined according to ATP-III criteria [1,2]; a diagnosis can be established when 3 of these risk factors are present: (1) waist circumference greater than 102 cm (40 in.) for men or greater than 88 cm (35 in.) for women, (2) TG level of 150 mg/dL or greater; (3) HDL cholesterol (HDL-C) level less than 40 mg/dL for men or less than 50 mg/dL for women, (4) blood pressure of 130/85 mm Hg or higher; (5) fasting glucose level of 110 mg/dL or greater. Subjects with diabetes were excluded from the MetSyn group, which is in concordance with the methodology of the ATTICA study [3,17].

Finally, we divided subjects with FCH into 3 subgroups: (1) MetSyn subgroup (according to the ATP-III criteria), (2) diabetic subgroup (glucose >125 mg/dL), (3) non-MetSyn subgroup.

2.2. Investigated parameters

Arterial blood pressure was measured 3 times with the subject in sitting position, after participants had rested at least 30 minutes. Blood pressure measurements were taken 3 times by a cardiologist, with the subject's right arm relaxed and well supported by a table, at an angle of 45° from the trunk (ELKA aneroid manometric sphygmomanometer, Von Schlieben, Munich, Germany). The systolic blood pressure level was determined by the first perception of sound (of tapping quality). The diastolic blood pressure level was determined by phase V when the repetitive sounds become fully muffled (disappeared). Changes in loudness were not considered. The mean value of 3 consecutive measurements of blood pressures was taken into account for the analysis that followed. Patients whose average blood pressure levels were greater than or equal to 140/90 mm Hg, who were under antihypertensive medication, or who were told by a physician that they had hypertension but were untreated, or subjects with MetSyn with blood pressure greater than or equal to 130/85 mm Hg were classified as hypertensives.

A 12-hour fasting and abstinence from alcohol and coffee preceded blood sample collection. Blood samples were collected between 8 and 10 AM from the antecubital vein of the individual who was kept in a seated position. The biochemical evaluation was carried out in the same laboratory that followed the criteria of the World Health Organization Lipid Reference Laboratories. All biochemical examinations (serum total cholesterol, HDL-C, TGs, etc) were performed by using a chromatographic enzymic method (Technicon RA-1000, Dade Boehringer, Mannheim, Marburg, Germany). For reasons of validity, an internal quality control was in place for assessing the validity of TC, TGs, and HDL-C assessment methods. The intra- and interassay coefficients of variation of cholesterol levels did not exceed 4%. We also measured apolipoproteins A-I (apo A-I) and apo B, as well as lipoprotein(a), Lp(a). by a latex-enhanced turbidimetric immunoassay (BNII, Dade and Behring, Germany).

LDL-C was calculated by using the Friedewald formula: (total cholesterol) − (HDL-C) − 1/5(TGs), which is valid for TG values less than or equal to 400. For determination of plasma fibrinogen, blood was anticoagulated with 3.8% trisodium citrate (9:1 vol/vol) and was analyzed by nephelometry (BNII, Dade and Behring).

All individuals were classified according to the fasting blood glucose level as: (*a*) normal (glucose level <110 mg/dL), (*b*) with impaired glucose tolerance (glucose level ≥110 and ≤125 mg/dL), and (*c*) diabetic (glucose level >125 mg/dL).

A detailed medical history, including sociodemographic characteristics (age, sex, mean annual income during the past 3 years, and years of education) and information about the frequency of consumption of various foods and other lifestyle habits, was obtained. Current smokers were defined

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